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## USE OF DIISOPROPYL FLUOROPHOSPHATE ("DFP") IN TREATMENT OF GLAUCOMA

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AND

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**D**IISOPROPYL fluorophosphate ("DFP") has been shown to have a marked and prolonged miotic effect, in normal men and animals<sup>1</sup> The miosis may be accompanied with spasm of accommodation and ciliary pain<sup>2</sup> These effects have been shown to be due entirely to the inactivation of cholinesterase and not to direct action on the iris and ciliary muscle<sup>3</sup> In this respect "DFP" is similar to physostigmine<sup>4</sup> and neostigmine,<sup>5</sup> but in its reaction with cholinesterase it is at least five and a half times as potent and much more persistent than physostigmine<sup>6</sup> "DFP" can also overcome the effects of atropine and homatropine on the pupil and ciliary muscle<sup>3</sup> Finally, "DFP" has been shown to resemble physostigmine in its influence on the intraocular tension of normal human eyes,<sup>1b</sup> differing, however, in that its effect is much more prolonged Occasional normal human eyes show a rise in intraocular tension with "DFP,"<sup>1c, 1d</sup> but the majority display a subnormal tension for several days after one local application of very dilute preparations of "DFP"<sup>7</sup>

From the Departments of Ophthalmology and Pharmacology of the University of Pennsylvania, under contract with the Medical Division, Chemical Warfare Service, Edgewood Arsenal, Md

1 (a) Mazur, A, and Bodansky, O J Biol Chem **163**:261, 1946 (b) Koelle, G, and Gilman, A Personal communication to the authors (c) Bowden, E, Horton, R G, Sober, H A, Hunt, C M, and Ferguson, R L Personal communication to the authors (d) Wallen, L, Horton, R G, and Sober, H A Personal communication to the authors (e) Adrian, E D, Kilby, B E, and Kilby, M Personal communication to the authors (f) Cullumbine, H Personal communication to the authors (g) Scholz, R Personal communication to the authors (h) Scholz, R, and Wallen, L J Personal communication to the authors (i) Loughlin, R C Personal communication to the authors

2 Wallen, Horton and Sober<sup>1d</sup> Cullumbine<sup>1f</sup> Scholz and Wallen<sup>1h</sup>

3 Leopold, I H, and Comroe, J H, Jr Effect of Diisopropyl Fluorophosphate ("DFP") on the Normal Eye, Arch Ophth, this issue, p 17

4 Anderson, H K Effect of Poisons upon the Iris, J Physiol **33** 156 and 414, 1905

5 Leopold, I H, and Comroe, J H, Jr Influence of Neostigmine on the Denervated Iris of Cats Proc Soc Exper Biol & Med **60** 382, 1945

6 Mackworth, J F Personal communication to the authors

7 Scholz and Wallen<sup>1h</sup> Loughlin<sup>1i</sup> Leopold and Comroe<sup>3</sup>

Physostigmine<sup>8</sup> and neostigmine<sup>9</sup> are also capable of producing elevated intraocular pressure in some normal eyes of animals and human subjects

Because of the prolonged effect of very dilute preparations of "DFP" when locally applied to the normal eye, it seemed advisable to test the efficiency of this agent in glaucomatous eyes. Its lack of irritant properties had already been demonstrated in rabbits in which after application of a single lethal or repeated sublethal doses of "DFP" to the eyes there were no signs of clinically or histologically demonstrable damage to the eye,<sup>12</sup> and even direct injections into the anterior chamber of 0.1 cc of 0.1 per cent "DFP" produced no permanent ocular damage.<sup>3</sup> Studies of the pharmacologic action of "DFP" in the human subject by Comroe and co-workers<sup>10</sup> indicated that little if any danger of systemic toxicity would be encountered from doses considerably larger than those used locally in the eye.

Because of the necessity of using these drugs over long periods, it was essential to employ a stable preparation of "DFP". Koelle's<sup>11</sup> studies indicated that "DFP" was stable in peanut oil but not in aqueous solutions. Ten normal subjects were therefore tested for tolerance to fresh peanut oil (Planter's) by irrigating the eyes with 3 to 5 cc of the oil twice daily for ten days. No subjective or objective signs of irritation were noted, the only effect was a slight blurring of vision for a few minutes following the instillation, due to the oily film.

The stability of solutions of "DFP" in oil and water was determined on normal rabbit eyes by the ability of these solutions to constrict the pupil. According to this test, a 0.1 per cent solution of "DFP" in peanut oil has maintained its potency for more than three months. The same concentration in water gradually lost its potency and was entirely without effect by the seventh day.<sup>3</sup>

In order to determine whether solutions of "DFP" in oil are as potent as aqueous solutions, 6 patients with normal pupillary phenomena were tested with 3 drops of 0.1 per cent "DFP" in oil in one eye and with 0.1 per cent "DFP" in water in the other eye. The pupils were measured in dim light. The eyes receiving "DFP" in water showed maximum constriction of the pupil a few minutes before those receiving "DFP" in oil, but the eventual degree and duration of effect on pupillary diameter and intraocular tension (which was significantly lowered for four to eight days) were the same in the two eyes.

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8 Duke-Elder, W. S. *Text Book of Ophthalmology*, London, Henry Kimpton, 1932, vol. 1, p. 518.

9 Kull, J. *The Use of Prostigmine in the Treatment of Glaucoma*, *Ophthalmologica* **104** 23, 1942.

10 Comroe, J. H. Jr., Todd, J., and Koelle, G. *The Pharmacology of "DFP" in Man*, to be published.

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USE OF DIISOPROPYL FLUOROPHOSPHATE ("DFP") IN  
TREATMENT OF GLAUCOMA

## METHOD

Fifty-two patients with glaucoma in one or both eyes were treated with "DFP" during a period of six months. These patients represent a total of 78 glaucomatous eyes. Whenever possible, intraocular tensions were measured throughout a preliminary twenty-four hour period, during which the patient received no miotic therapy. With almost all patients other miotic agents had been tried before "DFP" was used. All patients to be treated with "DFP" were admitted to the hospital for at least seventy-two hours, so that intraocular tensions could be watched throughout the entire period. Tensions were estimated with a Schiøtz tonometer, tetracaine hydrochloride (0.5 per cent) being used for topical anesthesia. Visual acuities and visual fields were tested, and ophthalmologic examinations were made weekly or biweekly on each patient. Gonioscopic examinations were made on those eyes in which miotic therapy failed. Only in the eyes in which tension was maintained at or below 30 mm of mercury and in which no loss of visual fields occurred were the tensions considered controlled.

Solutions of 0.005 per cent "DFP" in oil failed significantly to lower intraocular tension in the first 3 eyes with chronic simple glaucoma in which it was tried. Subsequent clinical trial indicated that 0.05, 0.1 and 0.2 per cent concentrations in oil are suitable for use in such eyes. When a 0.2 per cent solution was ineffective, little was gained by using stronger concentrations.

## RESULTS

The results are summarized in table 1. Certain comments should be made on these data. In 16 eyes of 13 patients<sup>12</sup> none of the miotics used (pilocarpine, physostigmine or "DFP") lowered the intraocular tension satisfactorily. The right eye of patient 45 proved on histologic study to have an intraocular growth, and that of patient 4 presented ophthalmoscopic evidence of an intraocular tumor but the patient refused to have enucleation. Patients 26, 34 and 42 had occlusion of the central retinal vein with secondary glaucoma and completely closed angles of the anterior chamber, according to gonioscopic examination. Patient 50 presented uveitis with secondary glaucoma and iris bombé following trauma. In patients 5, 37 (both eyes) and 38 (both eyes) the angles of the anterior chamber were too shallow for gonioscopic observation. The angles of the anterior chamber of patients 31 and 41 were only partly open. The left eye of patient 19 is also included in this series, as it responded partially, but not adequately, to treatment with "DFP" during a congestive phase.

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<sup>12</sup> Patient 4 (right eye), patient 5 (right eye), patient 19 (left eye), patient 26 (left eye), patient 28 (right eye), patient 31 (left eye), patient 34 (left eye), patient 37 (both eyes), patient 38 (both eyes), patient 41 (both eyes), patient 42 (right eye), patient 45 (right eye) and patient 50 (right eye).



TABLE 1—Comparison of Diisopropyl Fluorophosphate ("D

| Patient | Eye      | Age | Type of Glaucoma   | Previous Operation   | Visual Acuity with Correction | Tension Range Without Miotics (Schiotz) |                 | Former Miotic Therapy*  |
|---------|----------|-----|--|--|-------------------------------|---|-----------------|---|
|         |          |     |  |  |                               | Low est, Mm Hg                          | High est, Mm Hg |   |
| 1 J C   | OD<br>OS | 70  | Glaucoma following cataract extraction                                 | Combined intracapsular cataract extraction, both eyes (9/1939)   | 6/15<br>6/12                  | 25<br>22                                | 35<br>35        | Pilocarpine, 1%, alone and with physostigmine, 0.25%, 4 × daily |
| 2 H R   | OS       | 65  | Chronic simple glaucoma  | Elliot trephination (9/1941)<br>Elliot trephination (1/1944)   | 6/15                          | 47                                      | 60              | Pilocarpine, 1%, and physostigmine, 0.25%, 4 × daily            |
| 3 A H   | OD<br>OS | 58  | Glaucoma secondary to low grade uveitis                                | Combined cyclodialysis with iridectomy   | 6/22<br>6/12                  | 28<br>28                                | 35<br>41        | Pilocarpine, 1% and physostigmine, 0.25% 4 × daily              |
| 4 H W   | OD       | 45  | Intraocular tumor (not proved), unocular glaucoma                      | None   | Light perception              | 41                                      | 65              | Pilocarpine, 1%, and physostigmine, 0.25%, 5 × daily            |
| 5 G M   | OD       | 41  | Unocular chronic simple glaucoma—provocative test on left eye negative | None   | 6/60                          | 35                                      | 40              | Pilocarpine, 1%, and physostigmine, 0.25%, 6 × daily            |
| 6 M S   | OD<br>OS | 45  | Chronic simple glaucoma  | None   | 6/9<br>6/9                    | 25<br>25                                | 40<br>40        | Pilocarpine, 1%, 4 × daily                                      |
| 7 T H   | OD       | 59  | Chronic simple glaucoma  | None   | 6/15                          | 35                                      | 40              | Pilocarpine, 1% and physostigmine, 0.25%, 4 × daily             |
| 8 R R   | OD       | 60  | Chronic simple glaucoma  | Elliot trephination (1/1939) and 11/1939)  | 6/9                           | 25                                      | 35              | Pilocarpine 1% and physostigmine 0.25%, 4 × daily               |
| 9 I J   | OD<br>OS | 70  | Glaucoma following cataract extraction                                 | Extracapsular cataract extraction with iridectomy (5/1942)<br>Intracapsular cataract extraction with iridectomy (2/1943), cyclodialysis (5/1943) | 6/15<br>6/15                  | 25<br>25                                | 35<br>35        | Pilocarpine, 1%, 4 × daily<br>Pilocarpine, 1% 4 × daily         |
| 10 E B  | OD       | 61  | Glaucoma following cataract extraction                                 | Intracapsular cataract extraction with peripheral iridectomy (11/1944)   | 6/22                          | 35                                      | 41              | Pilocarpine, 1% and physostigmine, 0.25%, 4 × daily             |
| 11 P G  | OS       | 69  | Chronic simple glaucoma  | Elliot trephination (5/1944)   | 6/60                          | 30                                      | 35              | Pilocarpine, 1% and physostigmine, 0.25%, 4 × daily             |
| 12 M M  | OS       | 63  | Chronic simple glaucoma  | None   | 6/9                           | 22                                      | 35              | Pilocarpine, 1%, and physostigmine, 0.25%, 3 × daily            |
| 13 A M  | OD<br>OS | 72  | Chronic simple glaucoma<br>Chronic simple glaucoma                     | None   | 6/9†<br>6/9†                  | 25<br>25                                | 41<br>41        | Pilocarpine, 1% and physostigmine, 0.25%, 3 × daily             |
| 14 V F  | OD<br>OS | 53  | Chronic simple glaucoma<br>Chronic simple glaucoma                     | Elliot trephination (1935)<br>Elliot trephination (1935)   | Blind<br>6/9                  | 35<br>30                                | 40<br>35        | Pilocarpine, 1%, and physostigmine, 0.25%, 4 × daily            |
| 15 W M  | OS       | 71  | Post cataract extraction, iridocyclitis                                | Intracapsular cataract extraction with peripheral iridectomy   | 6/9                           | 40                                      | 45              | Physostigmine, 0.50% 2 × hr no influence                        |
| 16 E M  | OS       | 66  | Chronic simple glaucoma  | None   | 6/9                           | 22                                      | 30              | Pilocarpine, 1% t i d   |
| 17 C S  | OD<br>OS | 74  | Chronic simple glaucoma<br>Chronic simple glaucoma                     | None<br>None   | 6/9<br>6/12                   | 19<br>19                                | 28<br>28        | Pilocarpine, 0.5% t i d   |
| 18 E R  | OD       | 47  | Acute primary glaucoma, duration twenty hours when patient first seen  | None   | Hand movements                | 4/10/45                                 | 45 at 30 p m    |   |

\* Pilocarpine nitrate and physostigmine salicylate were used † Without correction

*DFP") and Other Miotic Agents in Treatment of Glaucoma*

| Tension Range Former Therapy (Schiotz) |                 | "DFP" Therapy   | Tension (Schiotz) Range with "DFP" Therapy |                                  | Visual Fields   | Period of Observations | Comment  |
|--|-----------------|---|--|----------------------------------|---|------------------------|--|
| Low est, Mm Hg                         | High est, Mm Hg |   | Low est, Mm Hg                             | High est, Mm Hg                  |   |                        |  |
| 19<br>16                               | 35<br>30        | 0.05% every 4 days  | 17<br>15                                   | 30<br>30                         | No significant change   | 6 mo                   | No subjective symptoms   |
| 35                                     | 41              | 0.05 or 0.1% 3 x daily  | 19   | 30                               | No significant change   | 5 mo                   | No discomfort from drops, but patient discontinued drug for two weeks, with considerable loss of field   |
| 28<br>28                               | 35<br>41        | 0.05 or 0.1% every 3 to 4 days  | 20<br>19                                   | 28<br>25                         | No significant change   | 6 mo                   | Slight brow ache during first week of therapy, none thereafter   |
| 41                                     | 65              | 0.05%, 1 instillation   | No change over 2 hr period                 |                                  | Not applicable  | One day                | Severe brow and eye ache   |
| 35                                     | 40              | 0.05%, 1 instillation   | No change over 2 hr period                 |                                  | Not applicable  | One day                | Severe brow and eye ache   |
| 19<br>19                               | 25<br>35        | 0.05 or 0.1% every 10 days, same every 4 days   | 13<br>13                                   | 22<br>26                         | No significant change   | 3 mo                   | Severe brow and eye ache, blurring of vision, patient discontinued use of drops because of these symptoms  |
| 35                                     | 40              | 0.1% every 3 days   | 17   | 26                               | No significant change   | 6 mo                   | No symptoms  |
|  |                 |   |  |                                  | No significant change   | 6 mo                   | Slight brow ache, considerable blurring of vision  |
| 19                                     | 35              | 0.1% every 2 days   | 16   | 28                               | No change   | 6 mo                   | No discomfort  |
| 25                                     | 30              | 0.1% every 4 days   | 17   | 19                               | No change   | 6 mo                   | No discomfort  |
| 25                                     | 30              | 0.1% every 4 days   | 17   | 19                               | No change   | 6 mo                   | No discomfort  |
| 35                                     | 41              | 0.1% 2 x daily  | 19   | 22                               | No change   | 6 mo                   | No discomfort  |
| 30                                     | 35              | 0.1% daily  | 23   | 30                               | No change   | 5 mo                   | No discomfort  |
| 22                                     | 30              | 0.1% every 5 days   | 16   | 23                               | No change   | 5 mo                   | Slight brow ache   |
| 25<br>25                               | 41<br>41        | 0.1% every 3 days   | 15<br>11                                   | 25<br>20                         | No change   | 3 mo                   | Severe eye and brow ache, patient discontinued drug because of these symptoms  |
| 30<br>22                               | 35<br>35        | 0.05%, 1 instillation every 3 days  | 20<br>15                                   | 30<br>30                         | Blind, recent loss with pilocarpine and physostigmine, no further loss with "DFP"   | 5 mo                   | After each application visual blurring for six hours, which does not prevent library work  |
| 40                                     | 40              | 0.1% "DFP", thereafter once every 2 days  | 32.5 in 20 min<br>30 in 1 hr<br>19 22      |                                  | No loss on "DFP"  | 3 mo                   | Slight brow ache for few hours after each instillation, drug discontinued, miotics no longer required  |
| 19                                     | 30              | 0.05%, 1 instillation every 5 days  | 16   | 22                               | No loss on "DFP"  | 3 mo                   | Visual blurring for 3 hr, barely perceptible ciliary flush, no flare or floaters, brow ache on one occasion, patient preferred frequent instillations of pilocarpine to discomfort of "DFP", so latter drug no longer used |
| 19<br>19                               | 23<br>23        | 0.05% every 4 days  | 16<br>16                                   | 25<br>25                         | Recent loss on use of pilocarpine in both eyes, no further loss on "DFP"  | 2 mo                   | Visual blurring for 6-8 hr after each instillation, fleeting ciliary flush, no flare or floaters, patient preferred frequent instillations of pilocarpine to discomfort of "DFP" so that drug was stopped                  |
|  |                 | 4/10/45 0.1% at 5 30 p m<br>Repeated at 7 30 p m<br>Repeated at 9 30 p m<br>Repeated at 12 midnight<br>4/11/45 6 00 a m<br>4 00 p m |  | 45<br>35<br>30<br>20<br>14<br>14 | Iridectomy performed at 4 p m (4/11/45), no field loss evident on 4/20/45, vision, 4/20/45, 6/9 with correction, vision, 8/13/45, 6/9 with correction | 4/10/45 (4 doses)      | Some eye ache, but severe only on first instillation   |

TABLE 1—Comparison of *Dusopropyl Fluorophosphate* ("DFP")

| Patient | Eye | Age | Type of Glaucoma  | Previous Operation  | Visual Acuity with Correction | Tension Range Without Miotics (Schiotz) |                 | Former Miotic Therapy *  |
|---------|-----|-----|---|---|-------------------------------|---|-----------------|--|
|         |     |     |   |   |                               | Low est, Mm Hg                          | High est, Mm Hg |  |
| 19 D G  | OD  | 64  | Chronic simple glaucoma                                 | Acute exacerbation (3/1944), iridectomy (1944)  | 6/15                          | 20                                      | 35              | Pilocarpine, 1% t i d  |
|         | OS  |     | Chronic simple glaucoma                                 | None  | 6/12                          | 19                                      | 30              | Pilocarpine, 1%, t i d   |
|         | OS  |     | Acute exacerbation                                      | None  | Hand movements                |   | 45              | Physostigmine, 0.5% every 15 min for 1 hr<br>Physostigmine, 0.5%, + pilocarpine, 1%, every hour for 4 hr daily   |
| 20 A R  | OD  | 54  | Chronic simple glaucoma                                 | None  | 6/12                          | 22                                      | 28              | Pilocarpine, 1%, 4 × daily   |
|         | OS  |     | Chronic simple glaucoma                                 | Operation refused   | 1/60                          | 40                                      | 60              | Pilocarpine and physostigmine, 0.25% 4 × daily   |
| 21 W L  | OD  | 71  | Chronic simple glaucoma                                 | None  | 4/100                         | 28                                      | 32              | Pilocarpine, 1% 3 × daily  |
|         | OS  |     | Chronic simple glaucoma                                 |   | 6/12                          | 25                                      | 35              | Pilocarpine, 1% 3 × daily  |
| 22 H T  | OD  | 57  | Glaucoma, post-cataract extraction                      | Intracapsular cataract extraction (1937)  | 6/9                           | 19                                      | 30              | Pilocarpine, 1%, 4 × daily   |
|         | OS  |     |   | Intracapsular cataract extraction (1938), cyclo dialysis (11/1939), (7/1940)                    | 6/60                          | 19                                      | 35              | Pilocarpine 1%, 5 × daily  |
| 23 E L  | OD  | 74  | Chronic simple glaucoma                                 | None  | 2/60 blind                    | 25                                      | 35              | Pilocarpine, 0.5%, 3 × daily   |
|         | OS  |     | Chronic simple glaucoma                                 | None  | 6/22 2 (?)                    | 19                                      | 28              |  |
| 24 S F  | OS  | 53  | Uveitis (Boeck's sarcoid), secondary glaucoma           | Iridectomy (4/1945)   | 6/60                          | 35                                      | 40              | Physostigmine, 0.5% 4 × daily  |
| 25 A W  | OS  | 65  | Secondary glaucoma, iridocyclitis following capsulotomy | Extracapsular cataract extraction (5/1944), capsulotomy (3/1945)                                | 6/100                         | 55 (on atropine)                        | 60              | Physostigmine, 0.5%, twice in 30 min   |
| 26 E T  | OS  | 70  | Glaucoma secondary to occlusion of central retinal vein | None  | Blind                         | 76                                      |                 | Physostigmine, 0.25%, every 15 min for 1 hr<br>physostigmine, 0.25% and pilocarpine, 1%, every hour for 4 hr<br>Physostigmine, 0.25%, and pilocarpine, 1%, 4 × daily |
| 27 S H  | OS  | 75  | Glaucoma secondary to intracapsular cataract extraction | Intracapsular cataract extraction with peripheral iridectomy (6/1943), cyclo dialysis (11/1943) | 6/100                         | 30                                      | 35              |  |
| 28 R E  | OD  | 60  | Absolute glaucoma                                       | None  | Blind                         | 65                                      | 70              | Physostigmine, 0.25%, and pilocarpine, 1% 4 × daily  |
|         | OS  |     | Chronic simple glaucoma                                 | Elliot trephination (5/1944), cyclodialysis (6/1944)  | 6/30†                         | 25                                      | 35              |  |
| 29 B H  | OD  | 41  | Chronic congestive glaucoma                             | None  | Blind                         | 35                                      | 40              | Physostigmine, 1%, 5 × daily, pilocarpine 0.5%, t i d  |
|         | OS  |     | Chronic simple glaucoma                                 | None  | 6/9                           | 22                                      | 30              |  |
| 30 R P  | OD  | 55  | Chronic simple glaucoma                                 | Cyclodialysis (4/1940)  | Blind                         | 25                                      | 40              | Pilocarpine, 1%, 4 × daily or physostigmine, 0.25%, 4 × daily, given alternately   |
|         | OS  |     | Chronic simple glaucoma                                 | Cyclodialysis (4/1940)  | Light perception              | 25                                      | 35              |  |
| 31 E B  | OD  | 74  | Chronic simple glaucoma                                 | None  | 6/12                          | 30                                      | 40              | Physostigmine, 1%, 4 × daily   |
|         | OS  |     | Chronic simple glaucoma                                 | None  | 6/9                           | 35                                      | 47              |  |

\* Pilocarpine nitrate and physostigmine salicylate were used † Without correction

# and Other Miotic Agents in Treatment of Glaucoma—Continued

| Tension Range Former Therapy (Schiotz) |                 | "DFP" Therapy   | Tension (Schiotz) Range with "D F P" Therapy |                 | Visual Field   | Period of Observations | Comment   |
|--|-----------------|---|--|-----------------|--|------------------------|---|
| Low-est, Mm Hg                         | High-est, Mm Hg |   | Low-est, Mm Hg                               | High-est, Mm Hg |  |                        |   |
| 30                                     | 35              | 0.05% 2 x daily   | 16   | 25              | No loss of field on use of "DFP" or of pilocarpine               | 4½ mo                  | No discomfort, eye ache with each instillation  |
| 19                                     | 30              | 0.1% "DFP," 1 in-<br>stillation<br>1 hr later   |  | 40              |  |                        |   |
| 40                                     |                 | 4 hr later  |  | 30              |  |                        |   |
| 40                                     |                 | 12 hr later   |  | 19              |  |                        |   |
|  |                 | 20 hr later   |  | 13              |  |                        |   |
|  |                 | "DFP" repeated  |  | 35              |  |                        |   |
|  |                 | 1 hr later, pilocarpine<br>and physostigmine  |  | 35              |  |                        |   |
|  |                 | 1 hr later  |  | 35              |  |                        |   |
|  |                 | Iridectomy performed  |  | 35              |  |                        |   |
|  |                 | Tension since without<br>miotic therapy   |  | 16              |  |                        |   |
| 17                                     | 28              |   | 19   | 22              | No loss  | 4½ mo                  | Blurred vision for 1-2 hr after each instillation   |
| 30                                     | 50              | 0.05% once daily  | 19   | 28              |  |                        |   |
| 22                                     | 28              | 0.05% once every<br>3 days  | 19   | 25              | No loss  | 4½ mo                  | Blurred vision for 6 hr after each instillation   |
| 22                                     | 28              |   | 19   | 28              |  |                        |   |
| 19                                     | 25              | 0.05% once every<br>7 days  | 16   | 22              | No loss  | 3 mo                   | On first instillation, marked ciliary flush, no flare or floaters in anterior chamber, flush not noted with subsequent instillations, patient bothered by redness of eyes and was greatly concerned with effects, drug was therefore stopped            |
| 19                                     | 28              | 0.05% once every<br>5 days  | 16   | 25              |  |                        |   |
| 22                                     | 35              | 0.05% once daily  | 16   | 30              | Recent loss with pilo-<br>carpine, no further loss<br>with "DFP" | 4½ mo                  | Blurring and some brow ache for 4 hr after each instillation  |
| 19                                     | 25              |   | 13   | 22              |  |                        |   |
| 30                                     | 40              | 0.05% once daily, use<br>discontinued after 4<br>days, with clearing of<br>hemorrhage in anterior<br>chamber, tension sub-<br>sided spontaneously | 22   | 30              |  | 4 days                 | Eye ache, quite severe for 12 hr after each instillation  |
| No benefit,<br>after 1½ hr<br>55       |                 | 0.05% 3 x daily in first<br>24 hr and thereafter<br>once daily, benefit<br>after first instillation<br>apparent in 15 min                         | 20   | 25              | No loss with "DFP,"<br>iridocyclitis not subsided                | 1 mo                   | Slight eye ache on initial doses, not with subsequent ones, drug discontinued after 1 mo, cyclodialysis performed   |
| 76                                     |                 | 0.1% every 2 hr for<br>8 hr   |  | 76              | Fields subsequently<br>reduced with iridencleisis                | 8 hr                   | Eye ache similar to that with physostigmine, perhaps slightly more severe   |
| 26                                     | 35              | 0.05% once daily  | 20   | 26              | No loss with "DFP"   | 4½ mo                  | Eye ache for 1 hr with first 2 instillations, much less with subsequent instillations, in last month no discomfort  |
| 48                                     | 75              | 0.05% once daily  | 40   | 48              | Blind  | 2½ mo                  | Some blurring of vision in left eye, no ache, but some ache in (blind) right eye, not noted on recent instillations, patient greatly concerned by blurred vision in left eye, visual field only 5 degrees about fixation, so that drug was discontinued |
| 22                                     | 30              |   | 22   | 30              | No loss with "DFP"   |                        | Ache in brow and eye on first day, visual blurring for 3 hr after each instillation, right eye enucleated after 2½ mo for cosmetic purposes   |
| 35                                     | 40              | Tension initially<br>lowered with 0.05%<br>"DFP" 4 x in 24 hr   | 13   | 16              | Blind  | 2½ mo                  |   |
| 19                                     | 25              | then 0.05% once daily,<br>0.05% once every 7 days   | 13   | 19              | No loss with "DFP"   | 4½ mo                  |   |
| 25                                     | 35              | 0.05% once daily  | 25   | 30              | Blind  | 3½ mo                  | No discomfort, patient uncooperative, so the drug was discontinued after 3½ mo trial  |
| 25                                     | 30              |   | 22   | 30              | No further loss  |                        |   |
| 30                                     | 35              | 0.05% twice daily   | 19   | 25              | No loss  | 4/16/45 to<br>6/2/45   | Ciliary injection and slight blurring in both eyes, conjunctival folliculosis from use of physostigmine cleared O D   |
| 40                                     | 47              |   | 25   | 35              | No loss  | 4/16/45 to<br>4/27/45  | Elliot trephination (6/2/45), patient disliked brow and eye ache and visual blurring in this eye O S Elliot trephination (4/27/45)  |

TABLE 1—Comparison of *Dusopropyl Fluorophosphate* ("DFP")

| Patient | Eye | Age | Type of Glaucoma   | Previous Operation            | Visual Acuity with Correction | Tension Range Without Miotics (Schiotz) |                 | Former Miotic Therapy *                                   |
|---------|-----|-----|--|-------------------------------|-------------------------------|---|-----------------|---|
|         |     |     |  |                               |                               | Low est Mm Hg                           | High est, Mm Hg |   |
| 32 M S  | O S | 65  | Chronic simple glaucoma  | None                          | Light perception              | 26                                      | 30              | Pilocarpine, 1% t i d                                     |
| 33 A B  | O D | 64  | Chronic simple glaucoma  | None                          | 6/12                          | 28                                      | 35              | Pilocarpine, 1%, 4 x daily                                |
|         | O S |     | Chronic simple glaucoma  | None                          | 6/15                          | 28                                      | 35              |   |
| 34 W D  | O S | 72  | Postvenous occlusion   | None                          | Blind                         | 55                                      | 60              | Pilocarpine 1% and physostigmine, 0.5% 5 x daily          |
| 35 J B  | O D | 58  | Absolute glaucoma  | None                          | Blind                         | 40                                      | 45              | Pilocarpine, 1% and physostigmine, 0.25% 4 x daily        |
|         | O S |     | Chronic simple glaucoma  | None                          | 6/12                          | 30                                      | 40              |   |
| 36 J D  | O D | 53  | Chronic simple glaucoma  | None                          | 4/60                          | 0                                       | 35              | Pilocarpine, 1% 5 x daily                                 |
|         | O S |     | Chronic simple glaucoma  | None                          | 3/60                          | 20                                      | 38              |   |
| 37 W D  | O D | 48  | Chronic congestive glaucoma  | None                          | 6/9                           | 40                                      | 58              | Pilocarpine 1%, and physostigmine, 0.5% and 1%, 5 x daily |
|         | O S |     | Chronic congestive glaucoma  | None                          | Hand movements                | 40                                      | 61              |   |
|         | O D |     | Chronic congestive glaucoma  | Basal iridectomy (5/22/45)    | 6/60†                         | 30                                      | 38              |   |
| 38 S W  | O D | 50  | Chronic congestive glaucoma  | None                          | 6/9                           | 35                                      | 40              | Pilocarpine, 1% and physostigmine, 0.5% 5 x daily         |
|         | O S |     | Chronic congestive glaucoma  | None                          | Blind                         | 45                                      | 51              |   |
| 39 J L  | O D | 48  | Chronic simple glaucoma  | Elliot trephination (1/1945)  | 6/9                           | 30                                      | 35              | Physostigmine, 2%, 4 x daily                              |
|         | O S |     | Chronic simple glaucoma  | Cyclodialysis (3/1945)        | 6/15                          | 30                                      | 40              |   |
| 40 E F  | O D | 58  | Glaucoma secondary to exfoliating lens capsule   | Elliot trephination (10/1944) | 6/30                          | 30                                      | 40              | Pilocarpine, 1% 5 x daily                                 |
| 41 J H  | O D | 39  | Chronic simple glaucoma  | None                          | 6/75                          | 45                                      | 56              | Pilocarpine, 1%, and physostigmine, 0.25% 4 x daily       |
|         | O S |     | Chronic simple glaucoma  | None                          | Hand movements                | 50                                      | 61              |   |
| 42 J W  | O D | 65  | Postvenous occlusion   | None                          | Blind                         | 40                                      | 58              | Physostigmine, 0.5%, pilocarpine, 1% 4 x daily            |
| 43 S N  | O D | 67  | Chronic simple glaucoma  | Iridectomy (3/25/44)          | 6/12                          | 25                                      | 40              | Pilocarpine, 2% 5 x daily                                 |
| 44 P D  | O D | 64  | Chronic simple glaucoma  | Elliot trephination (10/1944) | 6/61                          | 30                                      | 40              | Pilocarpine 1%, and physostigmine, 0.25% 5 x daily        |
| 45 J S  | O D | 65  | Glaucoma secondary to intraocular growth   | None                          | Light perception              | 50                                      | 60              | Physostigmine 0.5% and pilocarpine, 1%, 4 x daily         |
| 46 F M  | O S | 56  | Secondary to uveitis   | None                          | 6/20                          | 40                                      | 45              | No miotics, tried, only atropine 1% 2 x daily             |
| 47 J G  | O S | 46  | Chronic simple glaucoma  | None                          | 6/22                          | 27                                      | 41              | Pilocarpine 1% and physostigmine, 0.5%, 4 x daily         |
| 48 B A  | O D | 74  | Chronic simple glaucoma  | None                          | 6/15                          | 30                                      | 40              | Pilocarpine, 1%, and physostigmine 0.5% 4 x daily         |
|         | O S |     | Chronic simple glaucoma  | None                          | Light perception              | 30                                      | 47              |   |
| 49 L S  | O D | 55  | Chronic simple glaucoma  | None                          | 6/9                           | 26                                      | 35              | Pilocarpine 1%, and physostigmine, 0.5%, 5 x daily        |
|         | O S |     | Chronic simple glaucoma  | None                          | 6/20                          | 30                                      | 36              |   |
| 50 B T  | O D | 35  | Traumatic uveitis secondary glaucoma, iris bombe   | None                          | Light perception              | 40                                      | 45              | Pilocarpine 1% and physostigmine, 0.5% 4 x daily          |
| 51 R L  | O D | 60  | Chronic simple glaucoma  | None                          | 6/24†                         | 35                                      | 47              | Pilocarpine, 1%, 5 x daily                                |
|         | O S |     | Chronic simple glaucoma  | None                          | 6/24†                         | 30                                      | 47              |   |
| 52 M H  | O D | 45  | Secondary glaucoma trauma many years previously, aggravated by recent trauma, hemorrhage of anterior chamber | None                          | Light perception              | 67 On first visit within 1 hr           | 67              | Physostigmine 0.5%, hourly for 10 hr                      |

\* Pilocarpine nitrate and physostigmine salicylate were used † Without correction

and Other Miotic Agents in Treatment of Glaucoma—Continued

| Tension Range Former Therapy (Schiotz) |                 | "DFP" Therapy                             | Tension (Schiotz) Range with "DFP" Therapy |                 | Visual Field                               | Period of Observations | Comment   |
|--|-----------------|---|--|-----------------|--|------------------------|---|
| Low est, Mm Hg                         | High est, Mm Hg |   | Low est, Mm Hg                             | High est, Mm Hg |  |                        |   |
| 22                                     | 26              | 0.05% once every third day                | 13   | 20              | No loss                                    | 4 mo                   | Slight ciliary injection, no flare or floaters in aqueous   |
| 19                                     | 30              | 0.05% every 4 days                        | 13   | 22              | Slight loss in field                       | 4 mo                   | Slight blurring in both eyes, slight ciliary flush in first weeks of treatment, ciliary flush in past 2 mo  |
| 19                                     | 28              |   | 13   | 22              |  |                        |   |
| 55                                     | 60              | 0.1% 4 × daily                            | 40   | 50              | Blind                                      | 10 days                | No discomfort from "DFP," iridencleisis performed on left eye, with satisfactory lowering of tension and clearing of epithelial blebs   |
| 40                                     | 45              | 0.1% twice daily<br>0.1% once daily       | 22   | 30              | Blind eye                                  | 14 days                | Considerable blurring of vision, this alarmed patient, so that he desired to return to use of old drops (pilocarpine and physostigmine), has only 5 degree field about fixation in left eye |
| 22                                     | 35              |   | 13   | 22              | No change with "DFP"                       |                        |   |
| 22                                     | 30              | 0.1% once every 5 days                    | 13   | 22              | No change with "DFP"                       | 21 days                | Considerable eye ache and blurring of vision, patient returned to use of pilocarpine  |
| 25                                     | 30              |   | 13   | 19              |  |                        |   |
| 35                                     | 50              | 0.1%, 3 × daily                           | 30   | 50              | No change with "DFP"                       | 4 days                 | Discomfort similar to that of pilocarpine and physostigmine, same eye ache, iridencleisis, left eye, iridectomy, right eye, with satisfactory control of tension in left eye                |
| 40                                     | 61              | 0.1% 3 × daily                            | 35   | 58              | No further loss                            | 2 mo                   |   |
| 28                                     | 35              | 0.1% 3 × daily                            | 28   | 32              |  |                        |   |
| 30                                     | 35              | 0.1% 3 × daily                            | 30   | 35              | No change with "DFP"                       | 4 days                 | Severe ache in each eye, drug discontinued, iridencleisis, right eye, enucleation, left eye   |
| 45                                     | 51              |   | 45   | 51              |  |                        |   |
| 20                                     | 28              | 0.1% 2 × daily                            | 20   | 28              | No change with "DFP"                       | 10 days                | No discomfort from either physostigmine or M. G., return to physostigmine because patient could not be followed adequately  |
| 20                                     | 25              |   | 20   | 28              |  |                        |   |
| 30                                     | 35              | 0.05% once every 5 days                   | 17   | 23              | No change with "DFP"                       | 4 mo                   | No discomfort   |
| 22                                     | 47              | 0.1%, 2 × daily<br>0.1% 2 × daily         | 25   | 47              | No change with "DFP"                       | 5 days                 | Eye ache, blurring of distant vision, no improvement over that with physostigmine and pilocarpine, Elliott trephination on both eyes  |
| 22                                     | 45              |   | 22   | 40              |  |                        |   |
| 40                                     | 48              | 0.1% 3 × daily                            | 40   | 50              | Blind                                      | 3 days                 | No discomfort   |
| 25                                     | 35              | 0.05% once every 4 days                   | 16   | 22              | Not reliable                               | 3½ mo                  | Slight eye ache for 12 hr after each instillation during first 2 wk of treatment, no symptoms during last 2 mo  |
| 30                                     | 35              | 0.05% 2 × daily                           | 23   | 28              | No change with "DFP"                       | 3 mo                   | Considerable blurring of distant vision, eye ache   |
| 50                                     | 60              | 0.1%, one application in 24 hr            | 50   | 60              |  | Trial for only 1 day   | Severe ocular pain following instillation, duration several hours   |
| 45                                     | 47              | 0.1% 2 × daily                            | 13   | 19              | No loss                                    | 3 wk                   | Had only 2 applications of "DFP", uveitis subsequently quieted  |
| 25                                     | 41              | 0.1% once daily                           | 19   | 25              | No further loss                            | 2 mo                   | Some blurring of distant vision, slight ache for 30 min, patient in mental institution for 4 days without ocular treatment, after which he showed significant loss of field                 |
| 27                                     | 35              | 0.1% once daily                           | 16   | 23              | No further loss                            | 6 wk                   | Blurred vision, patient quite bothered by it  |
| 30                                     | 40              |   | 16   | 25              |  |                        |   |
| 26                                     | 35              | 0.1% once every third day                 | 13   | 19              | No further loss                            | 2 mo                   | Eye ache duration 12 hr, slightly blurred vision  |
| 26                                     | 32.5            |   | 13   | 26              |  |                        |   |
| 40                                     | 45              | 0.1% 3 × daily                            | 40   | 45              | Not under treatment with "DFP" long enough | Tried only 1 day       | Transfusion successfully lowered tension  |
| 41                                     | 47              | 0.1% once daily                           | 26   | 30              | No further loss                            | 2 mo                   | Brow ache, circumcorneal injection in both eyes for first six days of treatment, none since   |
| 35                                     | 41              |   | 16   | 22              |  |                        |   |
| 67                                     | 67              | 0.1% "DFP" 3 × in 24 hr, stopped in 48 hr | 22   | 30              | Not under treatment with "DFP" long enough | 1 mo                   | Paracentesis performed and anterior chamber cleared of hemorrhage after tension lowered by "DFP," use of "DFP" discontinued thereafter  |

In 24 eyes of 17 patients<sup>13</sup> pilocarpine, physostigmine or a combination of the two lowered intraocular tension to or below 30 mm of mercury. In all these eyes "DFP" lowered intraocular tension to the same or (usually) a lower level.

In 36 eyes of 29 patients<sup>14</sup> pilocarpine, physostigmine or a combination of the two failed to reduce the intraocular tension to within normal limits and to prevent further loss of visual fields. In each of these eyes "DFP" succeeded in lowering and maintaining the intraocular tension to or below 30 mm of mercury and prevented further loss of visual fields during the period of observation.

In 2 eyes (patient 18, right eye, and patient 46, left eye) no miotics other than "DFP" were tried. In both eyes "DFP" successfully lowered the intraocular tension. Patient 18 suffered an attack of acute primary glaucoma of the right eye, and a basal iridectomy was performed after the intraocular tension had been lowered. Patient 46 exhibited glaucoma secondary to uveitis, which subsequently subsided when the acute exacerbation of increased intraocular tension was controlled with "DFP."

In all the 60 eyes in which "DFP" successfully reduced the intraocular tension and in which pilocarpine and physostigmine were also tried, the duration of action of "DFP" greatly exceeded that of pilocarpine and/or physostigmine. The latter drugs were required at least three times a day and in many instances four, five or six times daily. "DFP," however, was required as often as three times daily in only 3 eyes<sup>15</sup>, twice daily in 7 eyes<sup>16</sup>, once daily in 17 eyes<sup>17</sup>, once every

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13 Patient 1 (table 1) (left eye), patient 6 (right eye), patient 9 (both eyes), patient 12 (left eye), patient 16 (left eye), patient 17 (both eyes), patient 20 (right eye), patient 21 (both eyes), patient 22 (both eyes), patient 23 (left eye), patient 28 (left eye), patient 29 (left eye), patient 30 (left eye), patient 32 (left eye), patient 33 (both eyes), patient 36 (both eyes) and patient 39 (both eyes).

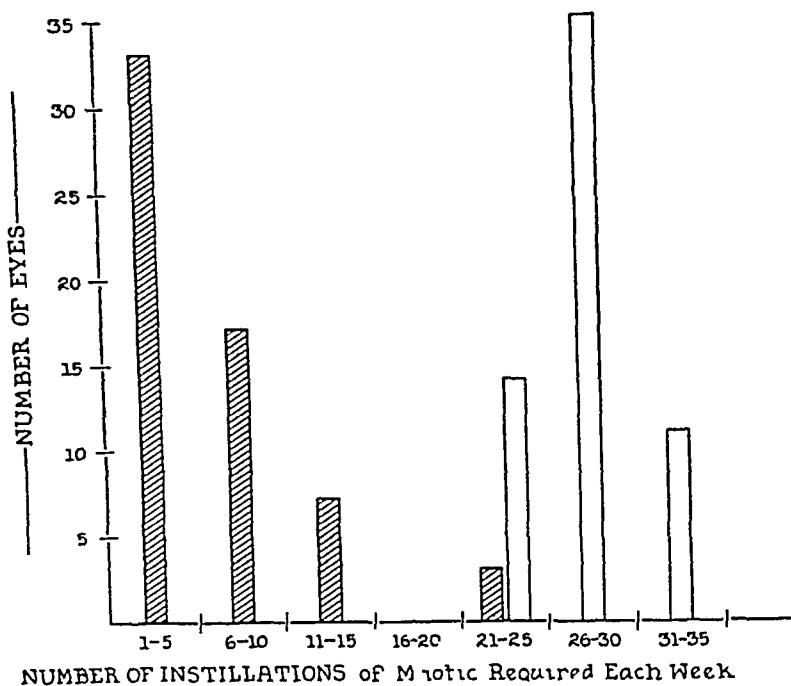
14 Patient 1 (right eye), patient 2 (left eye), patient 3 (both eyes), patient 6 (left eye), patient 7 (right eye), patient 8 (right eye), patient 10 (right eye), patient 11 (left eye), patient 13 (both eyes), patient 14 (both eyes), patient 15 (left eye), patient 19 (right eye), patient 20 (left eye), patient 23 (right eye), patient 24 (left eye), patient 25 (left eye), patient 27 (left eye), patient 29 (right eye), patient 30 (right eye), patient 31 (both eyes), patient 35 (both eyes), patient 40 (right eye), patient 43 (right eye), patient 44 (right eye), patient 47 (left eye), patient 48 (right eye), patient 49 (both eyes), patient 51 (both eyes) and patient 52 (right eye).

15 Patient 2 (left eye), patient 52 (both eyes).

16 Patient 10 (right eye), patient 19 (right eye), patient 31 (right eye), patient 35 (right eye), patient 49 (both eyes) and patient 44 (right eye).

17 Patient 11 (left eye), patient 20 (both eyes), patient 23 (both eyes), patient 24 (left eye), patient 25 (left eye), patient 28 (left eye), patient 29 (right eye), patient 30 (both eyes), patient 35 (left eye), patient 47 (left eye), patient 48 (right eye) and patient 51 (both eyes).

second day in 2 eyes<sup>18</sup>; once every third day in 12 eyes<sup>19</sup>, once every fourth day in 10 eyes<sup>20</sup>, once every five days in 6 eyes<sup>21</sup>, once every seven days in 2 eyes<sup>22</sup> and once every ten days in 1 eye<sup>23</sup>. These observations are summarized in the graph which shows clearly that the frequency of application of "DFP" was decidedly less than that required with pilocarpine and/or physostigmine.



Comparison of frequency of instillations required for the maintenance of intra-ocular tension in glaucomatous eyes using pilocarpine nitrate, 1 per cent, and/or physostigmine salicylate, 0.2-0.5 per cent, and using diisopropyl fluorophosphate ("DFP") 0.05-0.1 per cent.

The hatched rectangles indicate values for the eyes treated with "DFP", the clear rectangles, values for eyes treated with pilocarpine and/or physostigmine.

In the several instances in which the patient was returned to pilocarpine or physostigmine therapy after a trial of "DFP" no improvement in the effectiveness of the former drugs could be noted<sup>24</sup>. In this

18 Patient 8 (right eye), patient 15 (left eye)

19 Patient 3 (both eyes), patient 7 (right eye), patient 14 (both eyes), patient 21 (both eyes), patient 32 (left eye), patient 49 (both eyes), patient 13 (both eyes)

20 Patient 1 (both eyes), patient 6 (left eye), patient 9 (both eyes), patient 17 (both eyes), patient 33 (both eyes), patient 43 (right eye)

21 Patient 12 (left eye), patient 16 (left eye), patient 22 (left eye), patient 36 (both eyes) and patient 40 (right eye)

22 Patient 22 (right eye), patient 29 (left eye)

23 Patient 6 (right eye)

24 Patient 6 (both eyes), patient 13 (both eyes), patient 16 (left eye), patient 17 (both eyes), patient 22 (both eyes), patient 28 (both eyes), patient 35 (both eyes), patient 36 (both eyes) and patient 39 (both eyes)



respect "DFP" was unlike carbaminoylcholine chloride, which Clarke<sup>25</sup> found to enhance the effects of the two miotic alkaloids

Of all the 60 eyes in which the intraocular tension was maintained below 30 mm of mercury with "DFP" in only 2 (patient 33, both eyes) were slight but significant losses of the visual fields encountered. All other eyes retained the visual fields that they had possessed at the beginning of "DFP" therapy. The duration of observation is recorded in table 1. In patient 33 the visual fields were reduced. However, at no time while she was under therapy was the intraocular tension recorded above 22 mm of mercury, though the tension was recorded at various hours of the day and night during this patient's stay in the hospital and her clinic visits.

Careful attention was given to possible disadvantages of this miotic therapy. No evidence of local dermatitis or conjunctivitis has been noted from the repeated use of "DFP" to date. On the initial instillations pericorneal injection was frequently seen. This was rarely encountered after weeks of constant use.<sup>3</sup> No generalized systemic symptoms were noted by the patients after repeated use of "DFP". Information bearing on the systemic absorption of "DFP" was obtained from determinations of the blood cholinesterase after instillation of 0.1 per cent or 0.05 per cent "DFP" in peanut oil into the conjunctival cul-de-sac of 11 glaucomatous patients. The plasma cholinesterase was increased in 1 and lowered in 10 of the 11 patients. Five of the 10 patients showed a reduction of 10 per cent or less, the maximum decrease was 29 per cent. The cholinesterase content of the red blood cells showed no consistent changes in the 11 subjects. The second sample of blood was obtained one hour (1 patient), one and one-half hours (5 patients) and five hours (1 patient) after the instillation of "DFP" in both eyes. These changes, when compared with the daily fluctuations in normal persons, indicate either that no systemic absorption had occurred or that the amounts absorbed were too small to produce any significant general symptoms.<sup>3</sup>

Many of the patients complained of severe headache, brow ache, or a drawing or pulling eye ache after instillation of 0.05 or 0.1 per cent "DFP" (table 1). This sensation persisted for varying lengths of time. In addition, the majority of the patients were bothered with visual blurring, which was undoubtedly due to the ciliary spasm. Frequently these symptoms appeared only on attempted close work. Similar symptoms have been noted in normal eyes after instillation of "DFP".<sup>26</sup> Near point measurements and manifest refractions revealed that spasm

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25 Clarke, S. T. The Use of Doryl in the Treatment of Glaucoma, *Am J Ophth* 25:309, 1942.

26 Cullumbine.<sup>1f</sup> Scholz and Wallen.<sup>1h</sup> Leopold and Comroe.<sup>3</sup>

of accommodation was responsible. The false myopia was greatest within the first few hours after instillations of "DFP" and lessened gradually. As a result, it was not possible to prescribe an optical correction which would be satisfactory at all times. There was slight but insignificant lessening of the ciliary spasm with repeated use of the drug.

Nine of the patients, representing 17 glaucomatous eyes, were so bothered by one or more of these symptoms that they asked to be returned to their previous medication.<sup>27</sup>

*Summary*—Seventy-eight glaucomatous eyes of 52 patients were treated with "DFP." A summary of the results is given in table 2. It is evident that of the eyes with chronic simple glaucoma,

TABLE 2—*Comparison of Results of Treatment of Eyes with Various Types of Glaucoma Using Pilocarpine and/or Physostigmine and Using Diisopropyl Fluorophosphate ("DFP")*

| Type of Glaucoma                                     | No. of Eyes | Eyes Treated with Pilocarpine and/or Physostigmine |                      | Eyes Treated with "D F P" |                      |
|--|-------------|--|----------------------|---------------------------|----------------------|
|  |             | Tension Controlled                                 | Tension Uncontrolled | Tension Controlled        | Tension Uncontrolled |
| Acute primary  | 1           | Not tried  |                      | 1                         | 0                    |
| Chronic congestive                                   | 5           | 0  | 5                    | 1                         | 4                    |
| Chronic simple                                       | 48          | 21   | 27                   | 43                        | 5                    |
| Absolute   | 2           | 0  | 2                    | 1                         | 1                    |
| Glaucoma with exfoliating lens capsule               | 1           | 0  | 1                    | 1                         | 0                    |
| Glaucoma following occlusion of central retinal vein | 3           | 0  | 3                    | 0                         | 3                    |
| Glaucoma secondary to intraocular growth             | 2           | 0  | 2                    | 0                         | 2                    |
| Glaucoma after cataract extraction                   | 10          | 4  | 6                    | 10                        | 0                    |
| Glaucoma secondary to uveitis                        | 6           | 0  | 5                    | 5                         | 1                    |
| Totals   | 78          | 25   | 51                   | 62                        | 16                   |

pilocarpine and/or physostigmine was successful in controlling the intraocular tension in only 43.7 per cent. Of the same eyes, "DFP" was successful in keeping the tension below 30 mm. of mercury in 89.5 per cent. Of eyes in which glaucoma developed after cataract extraction, pilocarpine and/or physostigmine was successful in lowering an intraocular tension below 30 mm. of mercury in only 40 per cent, whereas "DFP" was successful in 100 per cent. It is interesting to note the greater effect of "DFP" in controlling the intraocular tension in the few eyes with glaucoma secondary to uveitis, but great significance cannot be attached to this small series. The great variability in the tension curve of eyes with glaucoma secondary to uveitis has

<sup>27</sup> Patient 6 (both eyes), patient 13 (both eyes), patient 16 (left eye), patient 17 (both eyes), patient 22 (both eyes), patient 28 (both eyes), patient 35 (both eyes), patient 36 (both eyes) and patient 39 (both eyes).

been noted by Kronfeld<sup>28</sup> It is possible that "DFP" therapy was started in a relatively favorable interval

#### RECOMMENDED THERAPY WITH "DFP" IN CASES OF GLAUCOMA

Experience with "DFP" has not been great enough to allow one to stipulate the exact method of administration in each case of glaucoma. However, the drug should not be ordered to be used empirically three times, or even once, a day. The frequency of application can be determined only by repeated checks of the intraocular tension throughout the first twenty-four hours and daily thereafter. As in the cases presented here, administration may be required only once daily, or even once weekly. The visual fields must be closely observed.

#### COMMENT

In the past decade several new drugs have been introduced into ophthalmology as therapeutic agents for glaucoma, namely, mecholyl and neostigmine,<sup>29</sup> carbaminoylcholine chloride<sup>30</sup> and furfuryl trimethyl ammonium iodide (Furmethide)<sup>31</sup>. Of these, neostigmine is the only anticholinesterase agent. None of these drugs has proved to be the answer to treatment of all forms of glaucoma, but each has a definite place and value in the therapy of this condition. "DFP," an anticholinesterase agent with a much more prolonged action than either neostigmine or physostigmine, also does not fulfil all the requirements of an ideal miotic antiglaucomatous agent, but it has certain attributes which entitle it to serious consideration.

In the first place, it is very effective. We have shown that "DFP" in concentrations of 0.05 to 0.1 per cent in oil will lower intraocular

28 Kronfeld, P. C. Gonioscopic Correlates of Responsiveness to Miotics, *Arch Ophth* **32** 447 (Dec.) 1944

29 Kull<sup>o</sup> Montalvan, P. Prostigmin in the Treatment of Glaucoma, *Am J Ophth* **26** 57, 1943. Clarke, S. T. Mecholyl and Prostigmin in the Treatment of Glaucoma, *ibid* **22**:249, 1938. Gifford, S. R. Treatment of Secondary Glaucoma, *Arch Ophth* **23** 301 (Feb.) 1940. Johnson, L. V. Newer Concepts in the Treatment of Glaucoma, *Ohio State M J* **37** 36, 1941.

30 Clarke<sup>25</sup> Velhagen, K., Jr. Action of Choline Bodies on Muscles of Iris Double Innervation, *Arch f Augenh* **108** 126, 1933. Practical Use of Carbaminoylcholine, *Klin Monatsbl f Augenh* **92** 472, 1934. Wilenkin, M. Effect of Carbaminoylcholine on Intraocular Pressure and on Width of Pupil, *ibid* **96** 84, 1936. O'Brien, C. S., and Swan, K. C. Carbaminoylcholine Chloride in the Treatment of Glaucoma Simplex, *Arch Ophth* **27**:253 (Feb.) 1942. Myerson, A., and Thau, W. Effect of Cholinergic and Adrenergic Drugs upon the Eye, *ibid* **18** 78 (July) 1937. Hardesty, J. F. The Use of Doryl in Glaucoma, *Am J Ophth* **27** 623, 1944.

31 Myerson, A., and Thau, W. Ocular Pharmacology of Furfuryl Trimethyl Ammonium Iodide, *Arch Ophth* **24**:758 (Oct.) 1940. Uhler, E. M. The Use of Furmethide in Comparison with Other Miotics for the Treatment of Glaucoma, *Am J Ophth* **26** 710, 1943.

tension even in glaucomatous eyes not satisfactorily maintained with aqueous solutions of 1 per cent pilocarpine nitrate or 0.25 to 0.5 per cent physostigmine salicylate. Another outstanding feature of this agent is the infrequency of application required. It is interesting to note that although 0.05 per cent "DFP" or weaker solutions in water or oil produced miosis which lasted one to two weeks on the average in normal human eyes, the duration of the miosis in glaucomatous eyes was much less than this. The longest miotic effect in any glaucomatous eye was twelve days, in patient 6 (right eye), and the shortest was twelve hours, in patient 2 (left eye). These observations suggest that there may be some fundamental derangement in the acetylcholine-cholinesterase system in glaucoma.

Six months may be an insufficient period in which to evaluate this therapy, and the value of "DFP" in long term therapy must still be determined. However, its proficiency in reducing intraocular tension over a period of months appears to be established by these data. It should also be borne in mind that the prolonged action of "DFP" may further be beneficial in reducing the fluctuations in tension that occur over each twenty-four hour period and thus in reducing the destructive effect of labile elevated ocular tension.

Although it is true that this agent does have certain disadvantages that preclude its universal use in antiglaucoma therapy, there are patients in whom the untoward effects are not troublesome and in whom in spite of these untoward effects "DFP" may prove to be of considerable value. Some of these uses may be indicated: 1 "DFP" produces little discomfort in patients with glaucomatous, aphakic eyes, and it appears to be a most effective agent in controlling the tension in such eyes.<sup>32</sup> 2 "DFP" is able to overcome the pupillary and accommodative effects of atropine and should prove of therapeutic value in preglaucomatous and glaucomatous eyes unfortunately and inadvertently treated with atropine. 3 "DFP" may be helpful in controlling the tension in eyes in which operation must be postponed and pilocarpine or physostigmine has proved ineffective. 4 "DFP" may properly be used initially in relief of acute congestive glaucoma, since

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<sup>32</sup> This action is difficult to explain. The ciliary muscle is intact in the aphakic eye, as in the eye with a lens, but the zonule fibers are relaxed and have no firm insertion in the aphakic eye. This suggests that intact zonule fibers must be present for the pain of ciliary spasm to develop. If this is so, one would expect ciliary pain when the zonule fibers are stretched. According to the Helmholtz theory of accommodation, these fibers are relaxed when the ciliary muscle is contracted. The Tscherning theory teaches that the zonule fibers are stretched during spasm of the ciliary muscle. The latter theory would explain the decidedly less degree of discomfort in the aphakic eye after instillation of "DFP" than in the intact eye, since in the aphakic eye the zonule fibers cannot be stretched.

it is a more powerful agent than physostigmine. In other words, this anticholinesterase agent can be used in eyes in which physostigmine formerly was employed.

#### SUMMARY

Diisopropyl fluorophosphate ("DFP") is an anticholinesterase agent capable of producing prolonged and marked parasympathomimetic effects in the eye.

"DFP" has successfully lowered intraocular tension in glaucomatous eyes in 0.05 or 0.1 per cent concentration in a peanut oil vehicle.

In the majority of the glaucomatous eyes treated with 0.05 or 0.1 per cent oily solutions of "DFP" the intraocular tension was controlled with decidedly fewer daily instillations than when either 1 per cent pilocarpine nitrate and/or 0.25 to 0.5 per cent physostigmine salicylate in water was employed.

In all glaucomatous eyes successfully treated with pilocarpine or physostigmine "DFP" was also effective and usually maintained the intraocular pressure at a lower level.

No instance of dermatitis or conjunctivitis due to repetitive use of "DFP" was encountered in the 78 eyes tested.

In 36 of the 78 glaucomatous eyes in which treatment with pilocarpine or physostigmine had previously failed, "DFP" succeeded in maintaining intraocular tension below 30 mm. of mercury.

"DFP" has several untoward and undesirable ocular effects, namely, visual blurring, brow ache and eye ache, spasm of accommodation and pericorneal injection.

A slight depressant effect on serum cholinesterase could be detected from ocular instillations of "DFP" in a few cases, but no systemic symptoms were elicited by ocular administration in any of the 52 patients treated.

The special usefulness of this drug in ophthalmology is discussed.

NOTE—Among the eyes treated with "DFP" since this paper was submitted there have been 2 which have shown a rise in intraocular tension after the instillation of "DFP". One of these eyes had chronic simple glaucoma and the other congenital glaucoma. The tension in the congenitally glaucomatous eye fell spontaneously after the initial rise following the use of "DFP". In the eye with chronic simple glaucoma an iridectomy ab externo had to be performed to bring the tension back to its former level. These observations must be kept in mind in starting "DFP" therapy with any patient.

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# EFFECT OF DIISOPROPYL FLUOROPHOSPHATE ("DFP") ON THE NORMAL EYE

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DURING the past few years many investigators<sup>1</sup> have studied the physiologic and pathologic effects of the fluorophosphates. Of these, the diisopropyl derivative ("DFP") has received most attention. It has been shown to be a powerful inhibitor of cholinesterase<sup>2</sup> and therefore has pronounced parasympathomimetic and nicotinic actions. It is much more potent than physostigmine in these respects. In the eye, "DFP" has been shown to produce prolonged and marked miosis, spasm of the ciliary muscle, false myopia and decrease in intraocular tension.<sup>3</sup> The ocular effects of "DFP" far outlast those produced by other known miotic agents. For example, miosis was found to last two days in the rabbit,<sup>4</sup> ten days to two months in the cat<sup>5</sup> and three to nine days<sup>3a</sup> and fourteen to twenty-seven days<sup>3b</sup> in man. The spasm of the ciliary muscle has been found to last three to seven days in man.<sup>6</sup> Because of the

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1 McCombie, H, Adrian, E D, Kilby, B A, and Kilby, M. Personal communication to the authors. Bowden, E, Horton, R G, Sober, H A, Hunt, G M, and Ferguson, R L. Personal communication to the authors. Wallen, L, Horton, R G, and Sober, H A. Personal communication to the authors. Adrian, E C, Kilby, B E, and Kilby, M. Personal communication to the authors.

2 (a) Mackworth, J F. Personal communication to the authors. (b) Koelle, G, and Gilman, A Z. Personal communication to the authors. (c) Mazur, A, and Bodansky, O. Personal communication to the authors.

3 (a) Scholz, R, and Wallen, L J. Personal communication to the authors. (b) Loughlin, R C. Personal communication to the authors. (c) Cullumbine, H. Personal communication to the authors.

4 Scholz, R. Personal communication to the authors.

5 Cattell, McK. Personal communication to the authors.

6 Scholz and Wallen<sup>3a</sup>. It is believed that the prolonged action of "DFP" is due to an actual destruction of the enzyme cholinesterase rather than to a temporary inhibition. Evidence for this concept is found in the observation that the time for the restoration of the original cholinesterase activity of the plasma is about the same as that for the regeneration of plasma proteins and that the

(Footnote continued on next page)

potentialities of this long-acting, powerful miotic agent in the treatment of glaucoma, further studies of its ocular pharmacologic properties were undertaken

Our studies were directed mainly toward investigating the mode of action of "DFP," the possibilities of systemic absorption from its local use in the eye and the problem of "DFP"—atropine antagonism. In the course of these studies, we had opportunity to confirm and extend previous observations of other investigators

## RESULTS

*A. Effects on Iris, Ciliary Muscle and Intraocular Tension*—In all species tested (rabbits, cats, dogs and man) we confirmed the previous reports of intense, prolonged miosis following instillation of "DFP" into the conjunctival sac. Quantitative species variations were found to exist, but the effect of the drug was most marked and prolonged in man, in whom maximal pupillary constriction occurred after instillation of 0.1 per cent "DFP" in water or in peanut oil<sup>7</sup> and some miosis persisted for six to twenty-seven days (table 1).<sup>8</sup> The miosis began within five to ten minutes and was maximal within fifteen to twenty minutes. The pupils constricted slightly more rapidly after instillation of "DFP" in water, though the intensity and duration of the response were approximately equal for the solutions in oil and in water. Lower concentrations of "DFP" have been employed in glaucomatous human eyes. No effect on size of the pupil was noted when concentrations below 0.01 per cent were used, and the lowest concentration which produced maximal pupillary constriction in some of these eyes was 0.05 per cent in oil.<sup>9</sup>

The speed and intensity of the pupillary response to 0.1 per cent "DFP," therefore, are equal to or greater than those reported for 1 per cent physostigmine salicylate and 5 per cent neostigmine bromide in man.<sup>10</sup> The duration of response to "DFP" is much greater than that of any other known miotic agent.

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time for the restoration of the cholinesterase activity of the red blood cells parallels that of the regeneration of the red cells (Koelle and Gilman<sup>2b</sup> Mazur and Bodansky<sup>2c</sup>)

7 Maximal constriction occurred in rabbits after instillation of 0.1 per cent "DFP" (in oil or water) and in cats and dogs after 1 per cent solution (in water)

8 The duration never exceeded forty-eight hours in rabbits (0.1 per cent concentration in oil or water), two to six days in cats (1 per cent in water) or two to ten days in dogs (1 per cent in water)

9 Leopold, I. H., and Comroe, J. H., Jr. Use of Diisopropyl Fluorophosphate ("DFP") in Treatment of Glaucoma, *Arch. Ophth.*, this issue, p. 1

10 Duke-Elder, W. S. *Text Book of Ophthalmology*, London, Henry Kimpton, 1932, vol. 1, p. 518. Kull, J. *Ophthalmologica* 104:23, 1942

TABLE 1—Effect of *Dusopropyl Fluorophosphate* ("DFP") on Size of Pupil in Man \*

| Patient | Sex | Age | Color of Eyes | Initial Size of Pupil, Mm | Oil or Water Solution | Size of Pupil Following Instillation of 0.1 per Cent "DFP," Mm, Days |     |     |     |      |      |      |      |  |   |  | Comment |
|---------|-----|-----|---------------|---------------------------|-----------------------|--|-----|-----|-----|------|------|------|------|--|---|--|---------|
|         |     |     |               |                           |                       | 2d   | 4th | 6th | 8th | 10th | 14th | 17th | 20th | 27th   |   |  |         |
| 1 L F   | M   | 56  | Hazel         | OS 3                      | Water                 | 1  | 2   | 2   | 2.5 | 2    | 2    | 2    | 2    | 2  | Blurred vision and headaches 2 days, ciliary injection 10 days    |  |         |
|         |     |     |               | OD 3                      | Oil                   | 1  | 2   | 2   | 2.5 | 2    | 2    | 2    | 2    |  |   |  |         |
| 2 R G   | M   | 20  | Blue          | OS 4                      | Water                 | 1  | 2.5 | 2.5 | 3.5 | 2    | 5    |      | 3    | Blurred vision and ciliary injection 2 days, headache 6 days |   |  |         |
|         |     |     |               | OD 4                      | Oil                   | 1  | 2   | 2   | 3   | 2    | 4    |      | 2.5  |  |   |  |         |
| 3 T H   | M   | 17  | Blue          | OS 3                      | Water                 | 1  | 3   | 4   | 4   | 3    |      |      |      | Headache, blurred vision and ciliary injection 2 days        |   |  |         |
|         |     |     |               | OD 3                      | Oil                   | 1  | 3   | 4   | 4   | 3    |      |      |      |  |   |  |         |
| 4 R S   | M   | 20  | Blue          | OS 3                      | Water                 | 1  | 2   | 2   |     |      |      |      |      | Blurred vision 6 days  |   |  |         |
|         |     |     |               | OD 3                      | Oil                   | 1  | 2   | 2   |     |      |      |      |      |  |   |  |         |
| 5 P S   | F   | 23  | Blue          | OS 5                      | Water                 | 1  | 2.5 | 3.5 | 4   |      | 4    | 4    | 4    | 5  | Ciliary Injection and pain in eyes 2 days, blurred vision 14 days |  |         |
|         |     |     |               | OD 5                      | Oil                   | 1  | 2   | 3   | 4   |      | 4    | 4    | 4    | 5  |   |  |         |
| 6 R C   | F   | 44  | Blue          | OS 5                      | Water                 | 1  | 1.5 | 2.5 |     | 2    | 3    | 3    | 2    | 3  | Pain and ciliary injection 2 days                                 |  |         |
|         |     |     |               | OD 5                      | Oil                   | 1  | 1.5 | 2.5 |     | 2    | 3    | 3    | 2    | 3  |   |  |         |

\* Three drops of 0.1 per cent "DFP" in oil was instilled at thirty second intervals into the right eye, and 3 drops of 0.1 per cent "DFP" in water, into the left eye. Patient 4 left the hospital at the end of six days, while his pupils were still constricted.



A more precise comparison of the speed and intensity of miosis produced by "DFP" and by neostigmine was made in cats and dogs. As shown in table 2, 1 per cent "DFP" usually produced more prompt and more pronounced miosis in cats than did 5 per cent neostigmine bromide. In all instances "DFP" produced much more prolonged miosis.

TABLE 2—*Comparison of Influence of 5 per Cent Neostigmine Bromide and 1 per Cent "DFP" on Size of Pupil of Cat and Dog*

|                                | Animal | Number | Onset of Miosis, Min | Minimal Size of Pupil, Min | Time for Minimal Size, Min |
|--------------------------------|--------|--------|----------------------|----------------------------|----------------------------|
| 5 per cent neostigmine bromide | Cat    | 14     | 10 49                | 1 5 8                      | 26 115                     |
|                                | Dog    | 7      | 5 10                 | 0 5 1                      | 20 37                      |
| 1 per cent "DFP"               | Cat    | 6      | 16 19                | 1 2                        | 15 40                      |
|                                | Dog    | 3      | 8 12                 | 1 3                        | 15 30                      |

than did neostigmine, since pupillary constriction produced by the latter never lasted as long as twenty-four hours.

In the present study we did not measure the effect of the ciliary muscle of normal eyes. However, data are presented in table 3 showing the refractive error before and after the instillation of "DFP" in 5 patients with glaucoma. In each patient "DFP" produced a false myopia which was maximal within one hour and gradually lessened in the

TABLE 4—*Influence of "DFP" on Intraocular Tension of Normal Human Eyes\**

| Patient | Eye | Tension, Mm Hg |                   |                   |                    |                    |                    |                     |
|---------|-----|----------------|-------------------|-------------------|--------------------|--------------------|--------------------|---------------------|
|         |     | Prior to "DFP" | 5 Min After "DFP" | 24 Hr After "DFP" | 4 Days After "DFP" | 6 Days After "DFP" | 8 Days After "DFP" | 27 Days After "DFP" |
| L F     | O D | 19             | 16                | 13                | 15                 | 17                 | 18                 | 18                  |
|         | O S | 19             | 17                | 13                | 15                 | 16                 | 19                 | 19                  |
| R G     | O D | 22             | 20                | 15                | 15                 | 15                 | 19                 |                     |
|         | O S | 20             | 19                | 13                | 15                 | 15                 | 20                 |                     |
| T H     | O D | 23             | 19                | 15                | 19                 | 20                 | 22                 |                     |
|         | O S | 19             | 17                | 11                | 19                 | 19                 | 20                 |                     |
| R S     | O D | 21             | 20                | 11                | 11                 | 15                 |                    |                     |
|         | O S | 21             | 20                | 13                | 13                 | 15                 |                    |                     |
| P S     | O D | 19             | 16                | 10                | 13                 | 13                 | 16                 | 19                  |
|         | O S | 18             | 16                | 10                | 13                 | 16                 | 17                 | 19                  |
| R C     | O D | 20             | 17                | 11                | 13                 | 15                 |                    | 19                  |
|         | O S | 20             | 18                | 11                | 13                 | 13                 |                    | 21                  |

\* The subjects and experimental conditions are the same as those presented in table 1.

next forty-eight hours. These data confirm the observations of Scholz and Wallen<sup>8a</sup> that "DFP" is capable of producing ciliary spasm.

Intraocular tension was recorded (Schiotz tonometer) in 6 normal persons before and after instillation of 0.1 per cent "DFP." The intraocular tension fell in all 12 eyes (table 4). A decrease could be detected within five minutes in 3 patients. The maximal depression occurred within twenty-four hours. It returned slowly to normal, and in eight days

TABLE 3—Influence of 0.05 per Cent "DFP" in Peanut Oil on Refractive Errors of Glaucomatous Eyes

| No     | Patient | Eye | Manifest Refractive Error |                       |                       |                       |
|--------|---------|-----|---------------------------|-----------------------|-----------------------|-----------------------|
|        |         |     | Before "DFP"              | 1 Hr After "DFP"      | 24 Hr After "DFP"     | 48 Hr After "DFP"     |
| 8 R R  |         | O D | -4.00 C + 1.00, ax 90     | -8.00 C + 1.00, ax 90 | -6.00 C + 1.00, ax 90 | -5.00 C + 1.00, ax 90 |
| 6 M S  |         | O D | + 25, ax 90               | -5.00 C + 25, ax 90   | -5.00 C + 25, ax 90   | -3.50 C + 25, ax 90   |
|        |         | O S | + 50, ax 90               | -5.00 C + 50, ax 90   | -3.00 C + 50, ax 90   | -1.75 C + 50, ax 90   |
| 12 M M |         | O S | +1.00 C + 37, ax 105      | -3.00 C + 37, ax 105  | -2.50 C + 37, ax 105  | -2.00 C + 37, ax 105  |
| 16 E M |         | O S | + 75 C + 75, ax 175       | -2.00 C + 75, ax 175  | -1.75 C + 75, ax 175  | -1.00 C + 75, ax 175  |
| 19 D G |         | O D | +1.75 C + 50, ax 160      | - 75 C + 50, ax 160   | +1.00 C + 50, ax 160  | +1.50 C + 50, ax 160  |

recovery was almost complete, though one eye showed a slightly lowered tension on the twenty-seventh day. These data are essentially the same as those reported by Scholz and Wallen,<sup>3a</sup> although these authors described a transient rise in 1 of 12 men examined after instillation of "DFP." The effects of "DFP" on glaucomatous eyes are recorded in detail elsewhere.<sup>9</sup> However, it is worthy of mention that intraocular tension was lowered in several eyes with previous iridectomy in which no noticeable pupillary constriction occurred. In the other eyes, the decrease in tension was accompanied with pupillary constriction.

As would be expected from these ocular effects, many patients complained of blurred distant vision, difficulty in adjusting from near to distant objects and aching of the brow and eye after instillation of "DFP." The ocular pain often became more severe with close work. These symptoms are due largely to ciliary spasm and have been noted previously.<sup>3a,c</sup> Further details are included in a report of observations on 52 patients with glaucoma treated with "DFP."<sup>9</sup>

*B Site of Action of "DFP" on Iris*—The site of action of "DFP" on the iris was investigated in order to determine whether the drug acts entirely by inactivation of cholinesterase or partly by direct action of "DFP" on the muscle of the iris. It has been shown by Anderson<sup>11</sup> that physostigmine constricts the pupil in normal cats but fails to do so after the ciliary ganglion has been removed and time allowed for degeneration of the postganglionic fibers. While these results have never been disputed so far as the iris muscle is concerned, some investigators<sup>12</sup> have produced evidence that physostigmine has a direct action on striated skeletal muscle. Similar experiments on the eye have not been recorded for "DFP."

*Methods* Cats were selected for these experiments, since complete ciliary ganglionectomy is extremely difficult in the dog and the rabbit. (We operated on 10 dogs, but in no instance were we able to obtain reactions consistent with a complete ciliary ganglionectomy that persisted over a period long enough for evaluation of all the drugs concerned.) Cats were anesthetized with sodium pentobarbital given intravenously or intraperitoneally. The hair was removed from the region of the left eye, the lids were sutured together, and an incision in the skin was made below and lateral to the orbit. A portion of the zygoma and the lateral wall of the orbit was removed. The conjunctiva and Tenon's capsule were opened, and the external rectus muscle was identified. This muscle was elevated by means of a retractor, and the ciliary ganglion was exposed. If difficulty was encountered, the nerve from the inferior oblique muscle was traced back to its branch which leads to the ciliary ganglion. The ganglion was grasped with a fine hemostat, all branches were severed, and the ganglion was removed. The incision was then sutured and the wound flushed with solution of penicillin. No wound infections occurred. Since the operation abolished

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11 Anderson, H. K. *J. Physiol.* **33** 156 and 414, 1905.

12 Brown, G. L., and Harvey, A. M. *J. Physiol.* **99** 379, 1941.

corneal sensitivity and secretions at least temporarily, the chief postoperative complication was desiccation and ulceration of the cornea. A number of cats had to be discarded for this reason.

In some cats the left superior cervical ganglion was also removed. This ganglion was extirpated completely after it was distinguished from the vagus ganglion at the level of the carotid sinus.

The criteria of a complete ciliary ganglionectomy were (a) dilation of the pupil on the side of operation, (b) failure of the iris to react to strong light, (c) sensitivity to 0.5 per cent pilocarpine nitrate and 20 per cent mechoyl bromide on the side of operation and (d) failure of 2 per cent physostigmine salicylate to constrict this pupil.

The solutions were freshly prepared from redistilled "DFP"<sup>13</sup>. Each sample had been sealed in a glass ampule and kept in the ice box until just before dilution. Although lower concentrations of "DFP" are miotic, a 1 per cent solution in water was employed in these experiments in order to attain a high concentration of the drug within the eye. Two drops (0.1 cc) was instilled into the lower conjunctival sac of the right eye and 3 drops (0.15 cc) in the left eye, in this manner we were sure that the amount of "DFP" received by the denervated iris was at least equal to and probably greater than the amount received by the normal iris. Pupillary sizes were measured with a millimeter rule in the dimmest light compatible with accurate reading (unless otherwise stated), this light was kept constant throughout the experiments. At no time were the cats exposed to bright sunlight. The 5 cats used in this experiment had been operated on eighteen to twenty-one days before instillation of "DFP".

**Results** In 4 cats, 1 per cent "DFP" in water had no effect whatever on pupillary size on the denervated side, the pupil remaining widely dilated throughout (table 5). In cat 6 the pupil constricted from a diameter of 12 mm to one of 7 mm. However, it is unlikely that this represents a direct action of the drug on the denervated muscle of the iris, since instillation of 1 per cent atropine sulfate promptly dilated the pupil fully, it more likely indicates an incomplete ganglionectomy.

The failure of the pupil on the ganglionectomized side to react is not due to decreased permeability of the cornea following the operation. It can be inferred from table 5 that the effect of "DFP" lasted as many days on the left side as on the right, for the following reason. While the pupil on the right (intact) side returned to its control size within fifty-two hours in 4 of the 5 cats, it remained abnormally sensitive to light for nine to thirteen days. This sensitivity to light is due, we believe, to a continued lack of cholinesterase in the iris muscle. Bright light in the eye reflexly increases the parasympathetic impulses to the normal iris and so increases the formation of acetylcholine at the nerve endings. Because of the increased acetylcholine and the decreased cholinesterase, the muscle contracts more strongly to light and relaxes more slowly in dim light. Since ciliary ganglionectomy interrupts the pathway of the

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<sup>13</sup> Obtained from the Medical Division, Chemical Warfare Service, Edgewood Arsenal, Md

light reflex, we could not use the same technic on the left (denervated) side, in order to determine the length of the anticholinesterase effect of "DFP" Therefore, local instillation of 1 per cent acetylcholine bromide was employed In each instance, after administration of "DFP" the left pupil constricted definitely after instillation of this concentration of acetylcholine, whereas before administration of "DFP," 10 per cent acetylcholine bromide was usually without effect<sup>14</sup> This reaction to acet-

TABLE 5—Effect of 1 per Cent "DFP" in Water on Size of Pupil (Mm) in Normal (O D) Eyes and in Eyes After Ciliary Ganglionectomy (O S) with Cervical Sympathetic Ganglions Intact\*

| Time   | Cat 3 |      | Cat 4 |      | Cat 6 |             | Cat 7 |      | Cat 8 |      |
|--|-------|------|-------|------|-------|-------------|-------|------|-------|------|
|  | O D * | O S  | O D   | O S  | O D   | O S         | O D   | O S  | O D   | O S  |
| Control                                      | 11    | 12   | 10    | 12   | 10    | 12          | 9.5   | 12   | 11    | 12   |
| 1% "DFP" in water—2 drops, O D, 3 drops, O S |       |      |       |      |       |             |       |      |       |      |
| 15 min                                       | 9.0   | 12   | 7.0   | 12   | 0.5   | 12          | 5.0   | 12   | 0.9   | 12   |
| 25 min                                       | 1.0   | 12   | 2.0   | 12   | 0.5   | 8           | 0.5   | 12   | 2.0   | 12   |
| 40 min                                       | 0.5   | 12   | 0.5   | 12   | 0.5   | 7           | 0.5   | 12   | 0.5   | 12   |
| 55 min                                       | 0.5   | 12   | 0.5   | 12   | 0.5   | 7           | 0.5   | 12   | 0.5   | 12   |
| 75 min                                       | 0.5   | 12   | 0.5   | 12   | 0.5   | 7           | 0.5   | 12   | 0.5   | 12   |
| 4 hr   | 1.0   | 12   | 1.0   | 12   | 1.0   | 7           | 0.5   | 12   | 0.5   | 12   |
|  |       |      |       |      |       | 1% atropine |       |      |       |      |
| 5 hr   | 1.5   | 12   | 2.0   | 12   | 4.0   | 12          | 0.5   | 12   | 1.0   | 12   |
| 22 hr  | 9.0   | 12   | 5.0   | 12   | 7.0   | 12          | 3.0   | 12   | 9.0   | 12   |
| 47 hr  | 11.0  | 12   | 10.0  | 12   | 9.0   | 12          | 7.0   | 12   | 10.0  | 12   |
| 52 hr  | 11.0  | 12   | 10.5  | 12   | 9.0   | 12          | 4.5   | 12   | 11.0  | 12   |
| 53 hr  | 11.0  | 12   | 11.0  | 12   | 10.0  | 12          | 8.0   | 12   | 11.0  | 12   |
| 3 days                                       | L S   | A Ch | L S   | A Ch | L S   | A Ch        | L S   | A Ch | L S   | A Ch |
|  | 11.0  | 12   | 10.0  | 12   | 10.0  | 12          | 8.0   | 12   | 11.0  | 12   |
| 6 days                                       | L S   | A Ch | L S   | A Ch | L S   | A Ch        | L S   | A Ch | L S   | A Ch |
|  | 11.0  | 12   | 10.0  | 12   | 10.0  | 12          | 8.0   | 12   | 11.0  | 12   |
| 9 days                                       | L S   | A Ch | L S   | A Ch | L S   | A Ch        | L S   | A Ch | L S   | A Ch |
|  | 11.0  | 12   | 10.0  | 12   | 10.0  | 12          | 9.0   | 12   | 11.0  | 12   |
| 13 days                                      | L S   | A Ch | L S   | A Ch | L S   | A Ch        | L S   | A Ch | L S   | A Ch |
|  | 11.0  | 12   | 10.0  | 12   | 10.0  | 12          | 9.0   | 12   | 11.0  | 12   |
| 19 days                                      |       |      | L S   |      | L S   |             | L S   |      | L S   | A Ch |
|  | 11.0  | 12   | 10.0  | 12   | 10.0  | 12          | 9.0   | 12   | 11.0  | 12   |

\* L S indicates that the eye was light sensitive, and A Ch that it was acetylcholine sensitive. Numbers above L S and A Ch refer to size of pupil before procedure.

ylcholine lasted nine to thirteen days. In other words, though different criteria were employed, it appears that the effect of "DFP" on the intact and on the denervated eye was equal in duration, and by inference the same amount of "DFP" reached each iris and exerted the same anticholinesterase action locally. It is concluded, therefore, that "DFP" in the concentrations used has no effect on the iris muscle itself.

"DFP" (1 per cent in water) was instilled into the eyes of a sixth cat, in which both the left ciliary and the left superior cervical ganglion were removed. Though the right eye responded to the drug with pro-

14 Even ganglionectomized eyes did not respond with miosis to 10 per cent acetylcholine bromide if "DFP" had not been instilled. This indicates that the tissues of the cat eye must be able to inactivate acetylcholine even in high concentration.

nounced miosis, the pupil of the left eye remained unchanged in size. It had been thought that a weak constrictor action of "DFP" exerted directly on the iris muscle might be obscured by the existence and opposition of tonic dilator sympathetic impulses. These results indicate that "DFP," in the concentration used, has no effect whatever on the iris during the period of complete denervation.

*C Effect of "DFP" on Homatropinized and Atropinized eyes*—The high potency of "DFP" made it appear likely that it could overcome the action of homatropine, or even that of atropine, on the eye. Consequently, we evaluated the "DFP"—homatropine antagonism in 5 young adults (18 to 23 years) and the "DFP"—atropine antagonism in 6 children (8 to 12 years) and 5 adults (17 to 54 years). In the first group (table 6) 3 drops of 4 per cent homatropine hydrobromide was instilled at fifteen minute intervals, one hour and fifteen minutes after the last drop, 2 drops of "DFP" in peanut oil was instilled into each eye. The eyes of the 6 children in the second group were atropinized in the following manner. One drop of 0.5 per cent atropine sulfate was instilled into each conjunctival sac. Another drop was instilled at intervals of twelve, sixteen, twenty-two and thirty-six hours. One hour and forty-five minutes after the last (fifth) drop of atropine sulfate, 2 drops of 0.05 per cent "DFP" in peanut oil was instilled into both eyes of 4 children, and 2 drops of a 0.1 per cent concentration of "DFP" in oil into both eyes of the other 2 children. The eyes of the 5 adults in the third group were atropinized by placing 2 drops of 1 per cent atropine sulfate at intervals of one minute into both eyes. One hour later, 0.1 per cent (2 patients) or 0.2 per cent (3 patients) of "DFP" in oil was instilled. In all these patients the pupils were measured at regular intervals and the near points determined with a Duane line, in the last 5 patients visual acuities also were measured, employing a Snellen test chart.

From the data recorded in table 6, it is evident that in every eye previously homatropinized or atropinized "DFP" constricted the pupil and augmented the accommodation. The intensity of the effect of the drug varied. In 0.05 per cent concentration it completely overcame the influence of 4 per cent homatropine hydrobromide on the ciliary body and the musculature of the iris. In the eyes of the children, 0.05 per cent "DFP" always augmented the accommodation and constricted the pupil, but the effect of the drug lasted only twenty-four to forty-eight hours. The 0.1 per cent concentration had a greater effect. In adults, 0.1 and 0.2 per cent, "DFP" overcame the effects of atropine and lasted six to nine days.

It is interesting to note that only 0.2 per cent solution of "DFP" was required to overcome the action of 1 per cent atropine sulfate on the muscles of the iris and ciliary body. The ability of "DFP" to antagonize

TABLE 6—Influence of "DFP" on Homotropized or Atropinized Human Pupils

| Patient * | Near Points, Cm |     |             |                          |                  |     |    |     |   |                               | Pupillary Size, Cm |                          |                  |     |   |   |   |   |   |  |
|-----------|-----------------|-----|-------------|--------------------------|------------------|-----|----|-----|---|-------------------------------|--------------------|--------------------------|------------------|-----|---|---|---|---|---|--|
|           | Age, Yr         | Eye | Con<br>trol | After<br>Cyclo<br>plegia | Time After "DFP" |     |    |     |   |                               | Con<br>trol        | After<br>Cyclo<br>plegia | Time After "DFP" |     |   |   |   |   |   |  |
|           |                 |     |             |                          | 1 Hr             | 1   | 2  | 3   | 4 | 5                             |                    |                          | 6                | 1   | 2 | 3 | 4 | 5 | 6 |  |
|           |                 |     |             |                          |                  |     |    |     |   | A Homatropinized Adult Eyes   |                    |                          |                  |     |   |   |   |   |   |  |
| 1 H H     | 23              | OD  | 11          | 40                       | 7                | 7   | 7  | 7   | 9 |                               | 45                 | 9                        | 25               | 25  |   |   |   |   |   |  |
| 2 A G     | 23              | OS  | 11          | 40                       | 7                | 7   | 7  | 8   | 9 |                               | 45                 | 9                        | 2                | 25  | 3 |   |   |   |   |  |
| 3 H A     | 18              | OS  | 10          | 45                       | 7                | 7   | 7  | 8   |   |                               | 4                  | 9                        | 1                | 2   | 3 |   |   |   |   |  |
|           |                 | OS  | 10          | 43                       | 7                | 7   | 7  | 7.5 |   |                               | 4                  | 9                        | 1                | 2   | 3 |   |   |   |   |  |
|           |                 | OD  | 9           | 50+                      | 8                | 8   | 8  |     |   |                               | 3.5                | 8                        | 1                | 1.5 |   |   |   |   |   |  |
| 4 R D     | 20              | OS  | 9           | 50+                      | 8.5              | 8   |    |     |   |                               | 3.5                | 8                        | 1                | 2   |   |   |   | 2 | 2 |  |
|           |                 | OD  | 10          | 45                       | 7.5              |     |    |     |   |                               | 5                  | 8                        | 1                | 2   |   |   |   |   |   |  |
|           |                 | OS  | 10          | 49                       | 7                | 7.5 |    |     |   |                               | 5                  | 8                        | 1                | 1   | 1 |   |   |   |   |  |
| 5 M H     | 19              | OD  | 9           | 50+                      | 7                |     | 7  | 7   | 8 |                               | 5                  | 7                        | 1                | 1   |   |   |   | 3 | 3 |  |
|           |                 | OS  | 9           | 50+                      | 7                |     |    |     | 8 |                               | 5                  | 7                        | 1.5              | 1.5 |   |   |   |   |   |  |
|           |                 |     |             |                          |                  |     |    |     |   | B Atropinized Children's Eyes |                    |                          |                  |     |   |   |   |   |   |  |
| 6 B B     | 10              | OD  | 6           | 50+                      | 10               | 10  | 12 |     |   |                               | 3                  | 9                        | 4                | 8   |   |   |   |   |   |  |
|           |                 | OS  | 6           | 50+                      | 20               | 20  | 23 |     |   |                               | 3                  | 9                        | 7                | 8   |   |   |   |   |   |  |
| 7 O J     | 12              | OD  | 6.5         | 50+                      | 9                | 12  |    |     |   |                               | 3                  | 9                        | 3                | 7   |   |   |   |   |   |  |
|           |                 | OS  | 7           | 50+                      | 25               | 25  |    |     |   |                               | 3                  | 9                        | 8                | 9   |   |   |   |   |   |  |
| 8 J C     | 9               | OD  | 5           | 50+                      | 20               | 20  |    |     |   |                               | 5                  | 9                        | 7                | 9   |   |   |   |   |   |  |
|           |                 | OS  | 6           | 50+                      | 12               | 12  |    |     |   |                               | 5                  | 9                        | 5                | 7   |   |   |   |   |   |  |
| 9 R S     | 10              | OD  | 5           | 50+                      | 10               | 10  |    |     |   |                               | 4                  | 9                        | 4                | 7   |   |   |   |   |   |  |
|           |                 | OS  | 5           | 50+                      | 20               | 20  |    |     |   |                               | 4                  | 9                        | 7                | 8   |   |   |   |   |   |  |
| 10 B R    | 10              | OD  | 5           | 50+                      | 6                | 6   |    |     |   |                               | 3                  | 9                        | 2                | 6   |   |   |   |   |   |  |
|           |                 | OS  | 5           | 50+                      | 6                | 6   |    |     |   |                               | 3                  | 9                        | 2                | 7   |   |   |   |   |   |  |
|           |                 | OD  | 5           | 50                       | 7                | 7   |    |     |   |                               | 3                  | 9                        | 1                | 5   |   |   |   |   |   |  |
| 11 G R    | 8               | OS  | 5           | 50                       | 6                | 7   |    |     |   |                               | 3                  | 9                        | 1                | 5   |   |   |   |   |   |  |
|           |                 |     |             |                          |                  |     |    |     |   | C Atropinized Adult Eyes      |                    |                          |                  |     |   |   |   |   |   |  |
| Patient † | Age Yr          | Eye | Con<br>trol | After<br>Cyclo<br>plegia | Time After "DFP" |     |    |     |   |                               | Con<br>trol        | After<br>Cyclo<br>plegia | Time After "DFP" |     |   |   |   |   |   |  |
|           |                 |     |             |                          | 1                | 2   | 3  | 4   | 5 | 6                             |                    |                          | 1                | 2   | 3 | 4 | 5 | 6 | 9 |  |
|           |                 |     |             |                          |                  |     |    |     |   | Near Points, Cm               |                    |                          |                  |     |   |   |   |   |   |  |
| 1 O B     | 17              | OD  | 9           | 40                       | 9                | 40  | 10 |     |   |                               |                    |                          |                  |     |   |   |   |   |   |  |
|           |                 | OS  | 8.5         | 44                       | 11               | 8   |    |     |   |                               |                    |                          |                  |     |   |   |   |   |   |  |





atropine should be of value in ophthalmology. Other drugs used at present for the purpose are not satisfactory. Histamine in strong concentration is a powerful miotic but, unfortunately, causes considerable chemosis and inflammation of the conjunctivas and lids and is very painful. In order for physostigmine to constrict an atropinized pupil and maintain such antagonistic miosis, it must be used in concentration equal to or greater than the concentration of atropine and must be used repeatedly. Even then, in many instances, it may fail to produce an antagonistic effect on the pupil. Pilocarpine and carbaminoylcholine are not so powerful as physostigmine. On the other hand, the present data show that "DFP" will constrict the atropinized pupil in one or two applications, in weaker concentrations than that of the atropine used, and that its effect will persist.

Normal eyes usually show circumcorneal injection after instillation of a drop of "DFP" in oil in concentrations as low as 0.5 per cent. This corneal injection, we believe, is due to the inability of ocular tissues to destroy acetylcholine. After inactivation of cholinesterase by "DFP," the acetylcholine, normally liberated by parasympathetic impulses, persists and spreads to neighboring vessels. None of the atropinized eyes showed this after instillation of "DFP," probably because atropine also antagonizes the effect of acetylcholine on vessels.

*D. Effect of "DFP" on Blood-Aqueous Humor Barrier in the Eye*—The rate of appearance in the aqueous humor of intravenously administered fluorescein or inulin has been employed as a measure of the rate of diffusion of substance through the capillary membrane.<sup>15</sup>

After the intravenous injection of fluorescein, a greenish discoloration normally appears in the pupillary region of the iris in two to four minutes. After ten to twelve minutes a faint cloud of green fluorescence gradually fills the pupillary area.<sup>15c</sup> In our experiments, we instilled 2 drops of 0.1 per cent "DFP" in oil in the right eye of 12 rabbits, the left eyes were used as controls. Twenty minutes later 0.75 cc of 5.5 per cent solution of sodium fluorescein per pound of body weight was injected intravenously in each rabbit. The fluorescence was always detected first and much more intensely in the eyes treated with "DFP" and persisted longer in these eyes. The increased permeability to fluorescein lasted less than twenty-four hours, even though the treated eyes were still miotic.

In 6 other rabbits 1 per cent physostigmine salicylate was placed in the left conjunctival sac and 0.1 per cent "DFP" in the right sac.

15 (a) Linksz, Q. *Arch f Augenh* **104** 264, 1931. (b) Gifford, H. Use of Fluorescein Intravenously as Aid to Ophthalmic Diagnosis and Treatment, *Arch Ophth* **24** 122 (July) 1940. (c) Swan, K., and Hart, W. *Am J Ophth* **23** 1311, 1940.

There were no significant differences in the rate of appearance, intensity of fluorescence or persistence of fluorescence in the two series of eyes

Five cubic centimeters of a 10 per cent solution of inulin was injected intravenously in 11 rabbits (table 7) fifteen minutes before to twenty-five minutes after instillation of "DFP" into one conjunctival sac. Aqueous humor (from both eyes) and samples of blood were withdrawn fifteen to fifty-eight minutes after instillation of "DFP" and these were analyzed for inulin by the method of Roe<sup>16</sup>. As shown in table 8, there are no significant differences between the two eyes in regard to diffusion of inulin from blood to aqueous humor.

TABLE 7—Amounts of Inulin in Blood and Aqueous Humor Following Its Intravenous Injection

| Rabbit Number | Time of Inulin Injection After "DFP" Instillation, Min | Time of Withdrawal of Blood and Aqueous, Min | Inulin Recovered, Mg per Cc |             |       |
|---------------|--|--|-----------------------------|-------------|-------|
|               |  |  | Aqueous                     |             | Blood |
|               |  |  | O S 2% "DFP"                | O D Control |       |
| 1             | 2  | 15   | 0.02                        | 0.22        |       |
| 2             | 3  | 30   | 0.05                        | 0.05        | 0.21  |
| 3             | 3  | 30   | 0.12                        | 0.34        | 0.29  |
| 4             | 15   | 30   | 0.09                        |             | 0.15  |
| 5             | 15   | 30   | 0.01                        | 0.01        | 0.19  |
| 6             | 15   | 30   | 0.1                         | 0.1         | 0.42  |
| 7             | 15   | 30   | 0.1                         | 0.12        | 0.42  |
| 9             | 8  | 50   | 0.14                        | 0.14        | 0.46  |
| 10            | 25   | 55   | 0.07                        | 0.09        | 0.32  |
| 11            | 24   | 58   | 0.07                        | 0.1         | 0.22  |
| 12            | —15  | 43   | 0.68                        | 0.79        | 0.49  |

These results indicate an increased permeability of the capillaries for fluorescein (a substance of low molecular weight) but not to inulin (a substance of high molecular weight). It is probable that this capillary change is due to arteriolar vasodilation (with consequent increase in capillary pressure) rather than to increased permeability in general, such as might occur after the use of histamine.

E *Systemic Absorption of "DFP" from the Eye*—It became evident from observations on cats and dogs that systemic effects may follow the instillation of "DFP" into the conjunctival sac. In 1 of 11 cats, "DFP" (2 drops of a 1 per cent aqueous solution instilled in each eye) produced systemic effects, such as salivation and muscle tremors. While such an effect was much less frequent after 1 per cent solution of "DFP" than after a 5 per cent solution of neostigmine bromide,<sup>17</sup> we felt that the question of systemic absorption should be investigated carefully in man. In several thousand instillations of "DFP" in man there has been no sub-

<sup>16</sup> Roe, J. H. J. Biol. Chem. **107** 15, 1934.

<sup>17</sup> In 6 of 11 cats, instillation of 2 drops of 5 per cent neostigmine bromide in water into each eye led to marked and often alarming symptoms of salivation, frothing, dyspnea, diarrhea, vomiting and muscular tremors.

jective or objective evidence of nicotinic action or parasympathomimetic hyperactivity. Nevertheless, determinations of plasma and red cell cholinesterase were performed on 11 patients before and one to two hours after instillation of "DFP" into the conjunctival sac. No significant fall in red cell cholinesterase occurred in any patient after this. Plasma cholinesterase decreased more than 10 per cent in 4 of the 11 patients, the maxi-

TABLE 8—*Plasma and Red Cell Cholinesterase Levels in Eleven Patients Before and After Instillation of 2 Drops of 0.2 per Cent "DFP" into Each Eye and in Five Control Subjects Who Received No Drug*

| Initials | Time                               | Plasma<br>Cholinesterase * | Per Cent Change<br>Plasma<br>Cholinesterase | Red Cell<br>Cholinesterase † |
|----------|------------------------------------|----------------------------|---|------------------------------|
| J C      | Before                             | 17.0                       | -16   | 10.2                         |
|          | 1½ hr after                        | 14.4                       |   | 11.2                         |
| D G      | Before                             | 10.8                       | -29   | 13.0                         |
|          | 1½ hr after                        | 7.7                        |   | 12.9                         |
|          | 5 hr after                         | 8.8                        |   | 12.9                         |
| H M      | Before                             | 18.4                       | -23   | 10.9                         |
|          | 1½ hr after                        | 14.2                       |   | 11.4                         |
| H T      | Before                             | 18.1                       | -3  | 15.8                         |
|          | 1½ hr after                        | 17.6                       |   | 15.0                         |
| B H      | Before                             | 16.6                       | -5  | 10.0                         |
|          | 1 hr after                         | 15.7                       |   | 10.3                         |
| R P      | Before                             | 13.2                       | -4  | 15.7                         |
|          | 1½ hr after                        | 12.8                       |   | 15.8                         |
| A R.     | Before                             | 17.6                       | -10   | 8.6                          |
|          | 2 hr after                         | 15.9                       |   | 8.6                          |
| E T      | Before (last drop 11 days ago)     | 9.0                        | -10   | 10.7                         |
|          | 2 hr after 4 instillations in 8 hr | 8.1                        |   | 12.3                         |
| F E B    | Before                             | 18.9                       | -23   | 11.9                         |
|          | 2 hr after                         | 14.5                       |   | 11.7                         |
| R B      | Before                             | 13.4                       | -10   | 12.4                         |
|          | 2 hr after                         | 11.9                       |   | 12.6                         |
| W D      | Before                             | 17.5                       | +7  | 10.1                         |
|          | 2 hr after                         | 18.3                       |   | 11.0                         |
| G N ‡    | 0 hr                               | 19.7                       | -7  | 11.5                         |
|          | 4 hr                               | 18.3                       |   | 10.6                         |
| A T ‡    | 0 hr                               | 6.4                        | -8  | 9.8                          |
|          | 4 hr                               | 5.9                        |   | 9.2                          |
| N S ‡    | 0 hr                               | 11.7                       | -9  | 9.9                          |
|          | 4 hr                               | 10.6                       |   | 10.2                         |
| B W ‡    | 0 hr                               | 17.1                       | +5  | 12.9                         |
|          | 4 hr                               | 17.9                       |   | 12.7                         |
| F G ‡    | 0 hr                               | 12.9                       | -13   | 10.8                         |
|          | 4 hr                               | 11.2                       |   | 10.7                         |

\* Values are expressed in micromols of carbon dioxide per thirty minutes (1:5 dilution)

† Micromols of carbon dioxide per thirty minutes (1:10 dilution)

‡ The last 5 subjects received no drug but are included as controls on the relative constancy of determinations of the cholinesterase

mal decrease being 29 per cent (table 8). The decrease in plasma cholinesterase in these 4 patients was greater than the fluctuations which occurred normally in the 5 control subjects. It has been shown<sup>2b,c</sup> that plasma cholinesterase is extremely sensitive to "DFP" in man and that red cell cholinesterase is much more resistant. In man plasma cholinesterase may be reduced to 2 to 10 per cent without any appreciable reduction in red cell cholinesterase. Despite a very low plasma cholin-

esterase, symptoms do not appear in man (after a single dose of "DFP") until the red cell cholinesterase is reduced to 70 to 80 per cent. It is evident, therefore, that minimal or insignificant absorption occurred from ocular instillation in these patients. This does not mean, however, that significant absorption will not follow the frequent, indiscriminate local use of "DFP."

*F Selection of a Vehicle for "DFP"*—Previous studies have shown that "DFP" is unstable in water but relatively stable in peanut oil. Since the existence of a stable preparation is of great importance for clinical use, we investigated more carefully the differences between oily and aqueous solutions. The period over which "DFP" in oil remains potent was measured by preparing a 0.1 per cent solution of "DFP" in peanut oil and instilling 2 drops of this into a rabbit eye each day for a week and thereafter once a week. The solution was kept in closed dropper bottles at room temperature. It has maintained its ability to constrict the pupil maximally for more than three months. A 0.1 per cent solution of "DFP" in water, prepared at the same time and tested in similar manner on the other eye of the same rabbit, began to lose its potency on the fifth day and was entirely without effect on the seventh day.

To determine whether the oily vehicle altered the rate, intensity and duration of the effect of "DFP" on the eye, a comparison of the effects produced by oily and by aqueous solutions was made in rabbit and in human eyes. Two drops of 0.01, 0.05 or 0.1 per cent "DFP" in peanut oil was instilled into one eye, and a similar dose of aqueous solutions (freshly prepared) into the other eye, of a series of 20 rabbits. There was no significant difference in the rate, intensity or duration of pupillary constriction in these eyes.

Similar experiments were carried out on 6 normal human subjects, using solutions of 0.1 per cent "DFP" in water and in oil (table 1). These results, again, failed to demonstrate a significant difference between the effects produced by the oily and those produced by the aqueous solutions of "DFP."

Some difference has been found in experiments on cats. A 0.2 per cent solution of "DFP" in water produced pupillary constriction which began sooner, lasted longer and was more intense than that produced by 0.2 per cent "DFP" in oil.

#### SUMMARY

1. Diisopropyl fluorophosphate "DFP" locally instilled in the eye in low concentrations will produce prolonged miosis, ciliary spasm, false myopia and decrease in intraocular tension. Quantitative species variations were found to exist, but the effects were most marked and prolonged in man.

2 A 1 per cent solution of "DFP" produced more prompt, pronounced and prolonged miosis than a 5 per cent solution of neostigmine bromide

3 "DFP" in the concentrations used has no direct effect on the iris muscle itself, since it failed to constrict the totally denervated cat iris. Its effects, therefore, are due entirely to inactivation of cholinesterase

4 A 0.1 per cent solution of "DFP" was able to overcome the cycloplegic effect in human eyes of 4 per cent homatropine hydrobromide, and a 0.2 per cent solution of "DFP," that of 1 per cent atropine sulfate

5 "DFP" was shown to increase the capillary permeability for fluorescein but not for inulin

6 A slight decrease in the plasma cholinesterase was noted after ocular instillation of "DFP," indicating that minimal systemic absorption occurred

7 No significant difference could be demonstrated between oil and water as a vehicle for "DFP" for ophthalmic use except that "DFP" is decidedly more stable in peanut oil than in water

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# VISUAL DISTURBANCES ASSOCIATED WITH HEAD INJURIES

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THE large number of head injuries observed in battle casualties provides the best material for study of the representation of various areas of the retina in the cerebral cortex. Few contributions have been made from injuries sustained outside of war periods.

Experimental determination of field defects by induced injuries is not feasible, for obvious reasons. One, therefore, must depend on lesions of the brain in human subjects studied at operation or at necropsy. From patients so studied one can draw certain conclusions concerning those who do not come to operation or to necropsy.

The two most significant papers on the subject are those by Holmes and Lister,<sup>1</sup> in 1916, and by Holmes,<sup>2</sup> in 1918, in which they reported their studies of disturbances of vision by cerebral lesions observed in British casualties in World War I.

Henschen,<sup>3</sup> in 1900, had pioneered with pathologic studies showing that the visual cortex lay in the occipital region, and he localized several areas as representing various portions of the retina.

In 1909 Inouye<sup>4</sup> reported the effects of injuries to the occipital lobe incurred in the Russo-Japanese War and pointed out that the macular center was at or near the occipital pole.

Marie and Chatelin,<sup>5</sup> in 1914, reported a similar series of cases. Riddoch<sup>6</sup> later published case reports which confirmed previous observations.

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Read before the Ophthalmic Club of Philadelphia, March 6, 1945

1 Holmes, G H, and Lister, W T. Disturbance of Vision from Cerebral Lesions, *Brain* **39** 34, 1916

2 Holmes, G H. Disturbances of Vision by Cerebral Lesions, *Brit J Ophth* **2** 253, 1918

3 Henschen. Sur le centre cortical de la vision, *Cong internat de méd, sect d'opht*, Paris, 1900, pt 9, p 232

4 Inouye. Die Sehstörungen bei Schussverletzungen der kortikalen Sehsphäre, nach Beobachtung von Verwundeten der letzten japanischen Kriege, Leipzig, W Engelmann, 1909

5 Marie, P, and Chatelin, C. Les troubles visuels dus aux lésions des voies optiques intracérébrales et de la sphère visuelle corticale dans les blessures du crâne par coup de feu, *Rev neurol* **27** 882, 1914-1915

(Footnotes continued on next page)

Moreau,<sup>7</sup> in 1918, discussed central field defects in a paper on occipital lesions. He divided the retina into three zones: those of fixation, distinction and perception, and stated the belief that cortical representation was similarly divided.

Morax<sup>8</sup> differentiated the fixation area and the macular area and stated that he had not found the fixation area affected in cases of unilateral lesions but did so when both occipital lobes were injured.

The lesions to be studied involved the chiasm, the optic radiations and the occipital cortex. The anatomy and physiology of the chiasmal fibers require no discussion. The geniculocalcarine pathway lies in the internal capsule behind the sensory fibers and internal to the auditory fibers. Fibers from the upper retinal quadrants lie dorsally, while fibers from the lower retinal quadrants lie ventrally. The macular fibers lie between these two bundles. To the best of present knowledge, the visual cortex occupies the medial surface of each occipital lobe from the occipital pole to the anterior end of the calcarine fissure. Posteriorly, the visual area extends a little onto the lateral surface of each occipital lobe. This area is thought to include representation of the fixation area. Opinion is divided as to whether there is bilateral cortical representation of the macular areas. The consensus is that each cortical macular center represents half of each macula, that is, the left cortex represents the right half of each fixation area and vice versa. This must be so as there is division of the fixation area of the field of each eye when the entire occipital cortex on one side is damaged. The so-called sparing of the macula is the rule with vascular disease but is less frequent with traumatic lesions. Sparing of the entire fixation area is less frequently found when the central field is closely studied. One then finds division of the fixation area rather frequent. There are three reasons for sparing of the fixation area: (1) this area of the cortex may escape from injury, (2) there are two blood supplies to the occipital cortex, the calcarine artery and the middle cerebral artery, and (3) patients may learn to use eccentric vision, particularly when the fixation area is divided. In cases of vascular accident only one of the two arteries is usually occluded, and hence sparing of fixation is the rule. In cases

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6 Riddoch, G. On the Relative Perceptions of Movement and a Stationary Object in Certain Visual Disturbances Due to Occipital Injuries, *Proc Roy Soc. Med (Sect Neurol)* **10** 13, 1916-1917.

7 Moreau, F. Sur les troubles de la vision maculaire produit par les lésions traumatiques de la région occipitales, *Ann d'ocul* **155** 357, 1918.

8 Morax, V. Discussion des hypothèses faites sur les connexions corticales des faisceaux maculaires, *Ann d'ocul* **156** 25, 1918.

of traumatic lesions both arteries may be damaged or the entire cortex destroyed

It is interesting to note that the cortical representation of the macula is rather large as compared with the area representing the more extensive peripheral portions of the retina. This is analogous to the large motor and sensory areas in the parietal cortex representing the finger and thumb as compared with the areas representing the trunk and the extremities

In the area striata the periphery of the retina is represented near the anterior end of the calcarine fissure. Lesions in this area usually include damage to the optic radiations, and few authentic cases have been recorded in which isolated injury to this area was present. One case of Holmes and Lister's, 2 of Scarlett and Ingham's<sup>9</sup> and cases 8 and 9 of the present series may represent such injuries, but damage to the radiations cannot be excluded in any of these cases. The upper portion of each retina is represented on the area above the calcarine fissure, while the lower portion of the retina is represented in the area below the calcarine fissure. When the area below the calcarine fissure is injured, one should see a defect in the upper fields of vision. The explanation for the infrequency of such defects is that wounds in this area often result in death because of injury to the cerebellum and large blood vessels

Traquair<sup>10</sup> stated that traumatic lesions of the optic nerve and occipital lobe are frequent, whereas trauma to the chiasm is rare, and that lesions in the geniculate pathway are more often vascular than traumatic in origin

Riddoch<sup>11</sup> and Holmes<sup>12</sup> have secured interesting data regarding the dissociation of visual perceptions due to injury to the occipital lobes. They pointed out that patients may see movement in the blind field and discussed the prognostic value of this phenomenon. They expressed the opinion that such lesions probably were located in the region of the supramarginal and angular gyri in the parietal lobe. While there is a suggestion in the histories of some of the cases here reported that such dissociations were present, this point has not been studied

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9 Scarlett, H. U., and Ingham, S. D. Visual Defects Caused by Occipital Lobe Lesions. Report of Thirteen Cases, *Arch Neurol & Psychiat* **8** 225 (Sept) 1922

10 Traquair, H. M. *An Introduction to Clinical Perimetry*, ed 4, London, Henry Kimpton, 1942

11 Riddoch, G. Dissociations of Visual Perceptions Due to Occipital Injuries with Especial Reference to Appreciation of Movement, *Brain* **40** 15, 1917, Visual Disorientation in Homonymous Half-Fields, *ibid* **58** 376, 1935

12 Holmes, G. H. Disturbance of Visual Orientation, *Brit M J* **2** 449 and 506, 1918



The following 12 cases represent a variety of defects in the visual field which can be traced to a known type and site of injury, with supporting evidence obtained from reports of the neurosurgeon and the roentgenologist

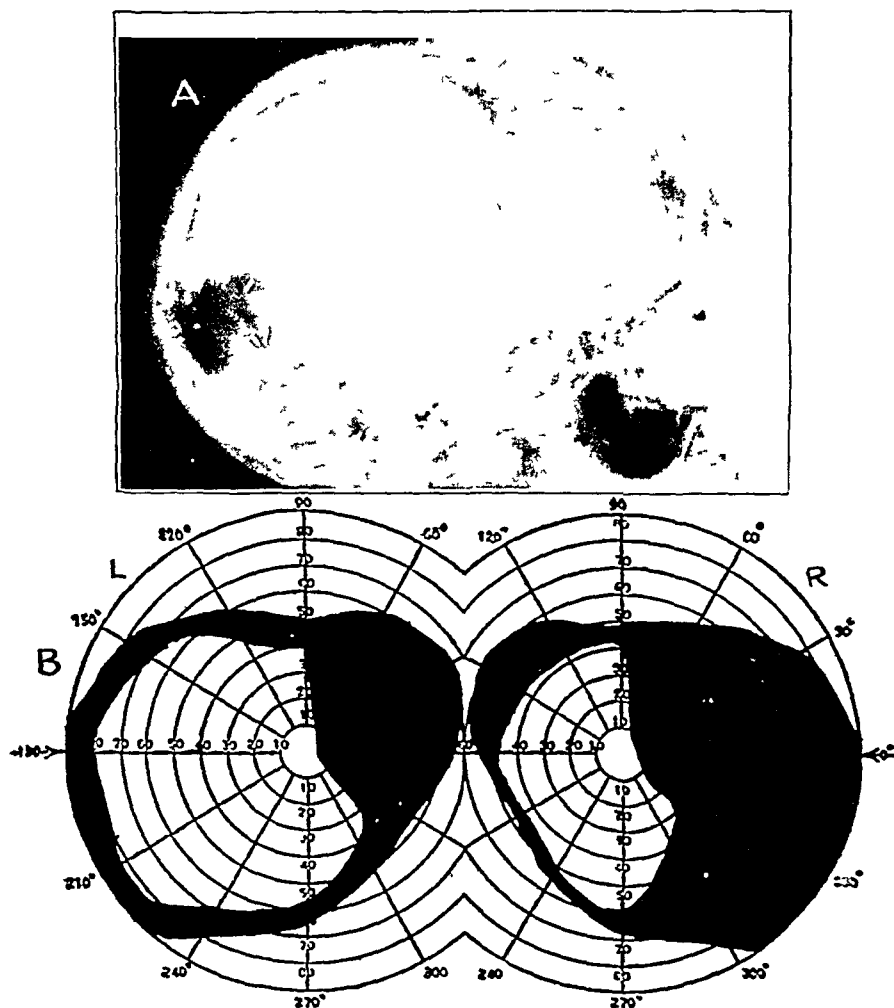


Fig 1—*A*, roentgenogram, *B*, visual fields taken with a 5 mm white test object. Visual acuity 20/15 in each eye.

In this figure, and in the accompanying figures, the visual fields are not plotted in the usual manner, owing to lack of proper cards at the time the charts were made. In some instances a card for the right eye was used for both eyes, but this should not detract from the reader's interpretation of the fields.

#### REPORT OF CASES

**CASE 1**—A white man aged 21 was wounded by a shell fragment Aug 7, 1944, sustaining a fracture in the left parieto-occipital region of the skull, with multiple depressed fragments of bone, laceration of the dura and brain and intracerebral clot.

Two days later craniotomy was performed, with repair of the dura with fascia lata. Healing was uneventful except for some drainage of the cerebro-

spinal fluid for about four weeks. There remained a palpable depression at the site of the injury.

A roentgenogram of the skull showed an oval area of bony dehiscence, measuring 5 by 3 cm, in the posterior portion of the left parietal bone and the anterior portion of the left leaf of the occipital bone. Three metallic clips were visible in this defect. A metallic shadow and an indefinite calcified mass measuring 1.5 by 1 cm were located 4 cm medial to the center of the bony defect.

The field defect was right homonymous hemianopsia, congruous with sparing of the fixation area and sparing of a small portion of the lower portion of the right field adjacent to the midline. Vision was 20/15 in each eye, with ability to read Jaeger type 1.

*Interpretation*—The site of injury, the data obtained at operation, the roentgenographic evidence and the field defect indicated a lesion of the left occipital cortex. Sparing of the fixation area was probably due to the dural blood supply by the calcarine artery and the middle cerebral artery. Another explanation always to be considered is fortuitous escape from injury of that portion of the area striata representing the fixation area, i. e., the posterior tip and the lateral surface of the occipital pole.

CASE 2—A white man aged 24 was wounded by fragments of an 88 mm shell on June 15, 1944, sustaining a compound, depressed fracture of the skull, with injury to the brain in the right temporoparietal area, a retained metallic foreign body in the left occipital lobe of the brain and complete hemianesthesia, with no loss of motor function.

On the day of injury the shell wound in the skull and brain was debrided, bleeding from the temporal artery, the middle meningeal artery, the temporo-occipital veins and the severed inferior petrosal sinus was arrested. Lacerated, contused dura and brain tissue from the temporal and occipital lobes was removed with suction. A graft of fascia lata was used to close the defect in the dura. Large sections of bone had to be removed in order to elevate the depressed fracture and to control bleeding. The patient was given 3,000 cc of blood because of severe hemorrhage. No pulse or blood pressure was elicited for forty minutes. Five hours after operation the blood pressure was 120 systolic and 80 diastolic.

This soldier was unconscious from the time of injury until at least two weeks later, when he found he was totally blind, that he could move his left arm and leg, although he had no sense of position, and that he had loss of sensation over the left side of his body. There was no speech defect, and no personality changes were noted.

Roentgenographic examination showed an extensive comminuted fracture of the right temporoparietal area, with a large separated fragment in the upper occipital area. A metallic fragment measuring 5 by 4 mm was present at the site of entrance, and a foreign body 10 by 15 mm was present in the left occipital lobe. Roentgenographic examination on August 28 showed the following condition: "A large bony defect on the right side involved the posterior half of the parietal bone, the temporal bone, the upper margin of the mastoid and a small portion of the adjacent occipital bone, with two radiating linear fractures through the occipital bone. A metallic foreign body measuring 2.3 by 1.3 by 0.7 cm was present in the left occipital lobe 1.5 cm to the left of the midline and 1.5 cm deep to the inner table."

Electroencephalographic examination showed an abnormal record indicative of damage to the right occipital and parietal areas

On September 7 a tantalum plate measuring 11.5 by 11.5 by 14 cm was inserted to cover the bony defect in the skull

The field defect was left homonymous hemianopsia with division of the fixation area. Vision was limited to light perception in the right eye and was 2/200 in

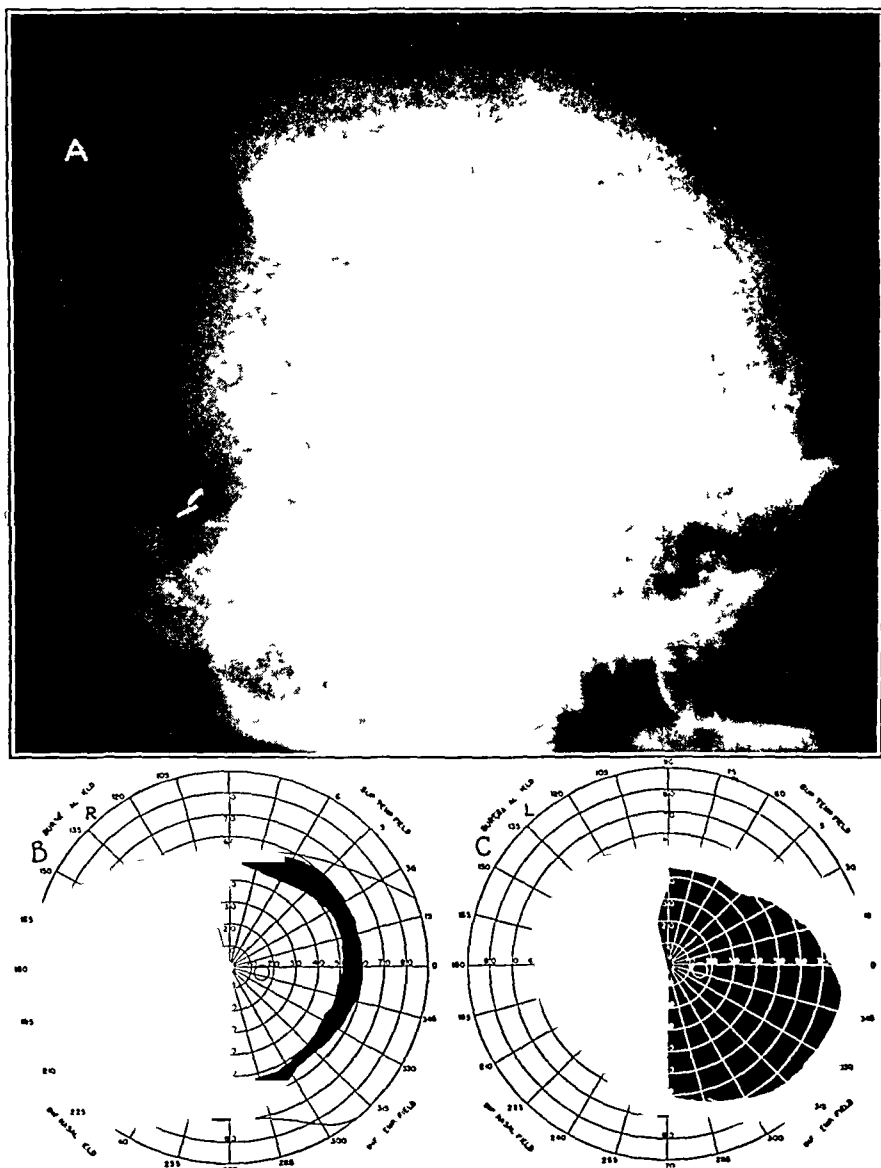


Fig 2—*A*, roentgenogram, *B* and *C*, visual fields of right and left eyes, respectively, taken Oct 30, 1941 with a 15 mm test object at a distance of 330 mm. Visual acuity 1/200 in each eye

the left eye. Reduction in vision may have been due in part to extensive hemorrhages in the vitreous of each eye. No lesions were visible in the fundus. There was no direct injury to either eye. The hemorrhages are to be explained by a

sudden increase in intracranial pressure and consequent compression of the vaginal space of the optic nerves and bleeding from the central veins

*Interpretation*—Injury to the right occipital and parietal lobes by penetration of a foreign body accounts for the left homonymous hemianopsia and left hemianesthesia and the mild left hemiplegia. The field

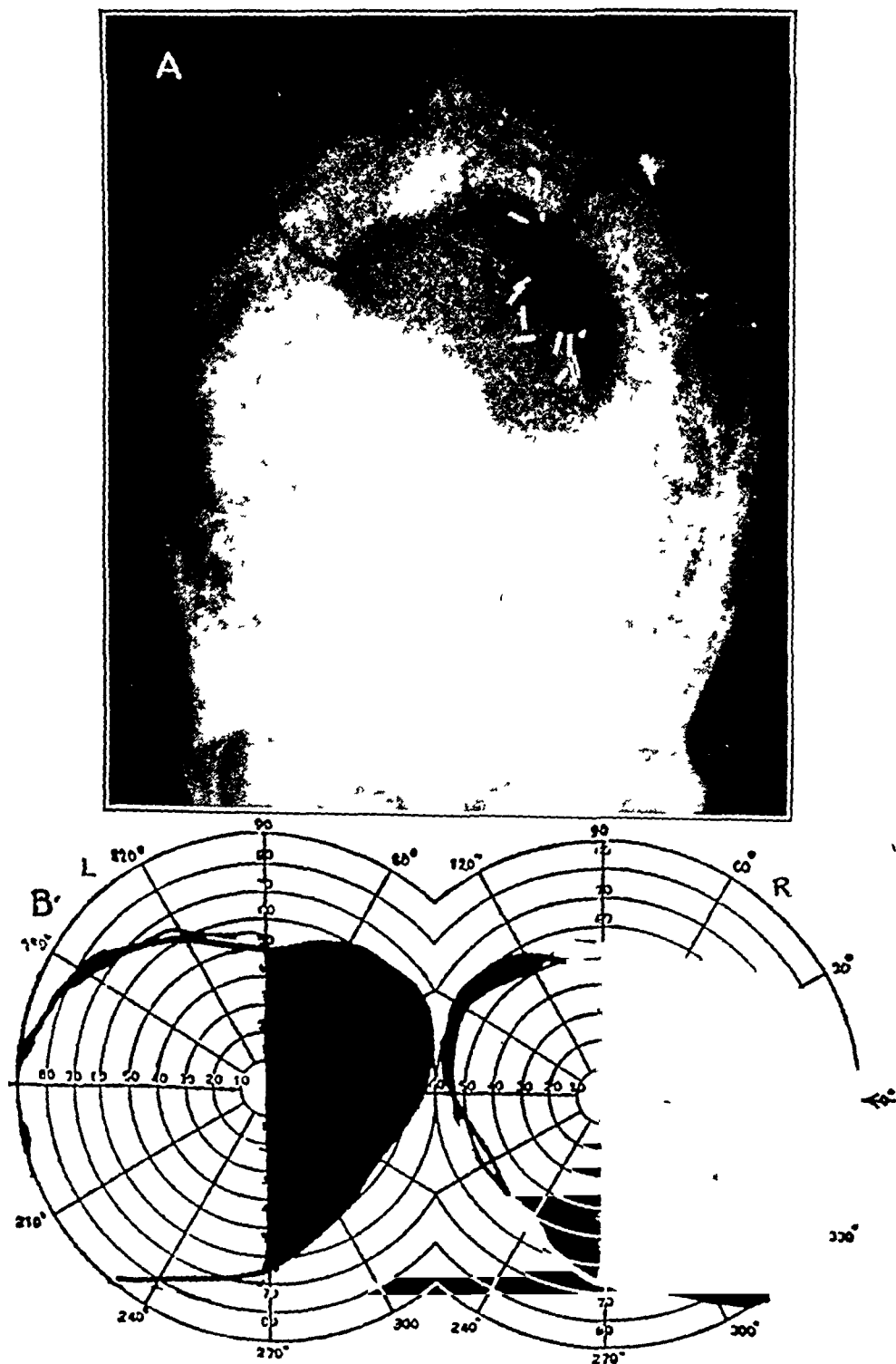


Fig 3—A, roentgenogram, B, visual fields taken with a 3 mm white test object. Visual acuity right eye, 20/70—1, with pinhole disk, 20/70—1, left eye, 20/200, with pinhole disk, 20/200

defect was noted as early as Aug 11, 1944 and has remained unchanged, although the hemorrhage in the vitreous has been largely absorbed. The foreign body in the left occipital lobe apparently did not damage the visual fibers or the cortex.

**CASE 3**—A white man aged 23 was wounded by shell fragments Sept. 26, 1944, sustaining a severe compound, comminuted fracture of both leaves of the occipital bone, with extensive stellate fractures of both parietal bones, multiple metallic foreign bodies were seen at a depth of 5 to 6 cm in the left parieto-occipital area.

The next day craniotomy was performed. Wide debridement, including removal of fragments of bone, was carried out, leaving a defect 6 by 3 cm in the occipital bone. The dura to the left of the midline was torn, and there was a subdural hematoma. Damaged brain tissue and the hematoma were removed, and the track of the foreign body in the left occipital lobe was irrigated, but the foreign bodies were not removed. The dural defect was closed with a pericranial graft, and the defect in the scalp was closed with a sliding flap.

Examination prior to operation revealed no light perception in either eye, but both pupils reacted to light.

The patient remained apparently blind for fifteen days, when he was found to have light perception. He also exhibited sensory aphasia and generalized hyperreflexia.

Bilateral papilledema was present for a considerable length of time but subsided, leaving yellowish nerve heads with absence of physiologic cupping.

Roentgenographic examination of the skull showed a semilunar defect measuring 4 by 8 cm in the occipital bone, the larger portion lying to the left of the midline. Linear fracture lines extended in all directions from this defect, and a Y-shaped fracture extended upward from the greater wing of the sphenoid bone on the right. Two large foreign bodies were present in the brain near the left parietal bone 9 cm above the mastoid process.

The field defect was right homonymous hemianopsia with division of the fixation area. Visual acuity was as follows: right eye, 20/70 + 2, left eye 20/100 + 1, with correction. He read Jaeger type 12 with each eye, with correction. Degenerative changes secondary to prolonged papilledema were present in each macular area. This accounts for the poor visual acuity.

*Interpretation*—The injury to the occipital region, with a tract of foreign bodies through the occipital and parietal lobes, together with the data obtained at operation, the roentgenographic evidence and the field defect, indicates damage to the left occipital cortex and the deeper tissue of the brain. The sensory aphasia and hyperreflexia indicate damage to the parietal lobes. In June 1945 vision was 20/50 —1 in each eye, with ability to read Jaeger type 9. There was no papilledema. The disk was still yellowish.

**CASE 4**—A white man aged 29 was wounded by a high explosive shell July 11, 1944, sustaining a depressed, compound, comminuted fracture in the left parieto-occipital region with damage to the dura and brain.

The next day craniotomy was performed. Multiple depressed fragments of bone, hair, dirt and soft brain tissue were removed. The dural defect was repaired with pericranium.

There was a transient palsy of the sixth nerve. The pupils reacted to light. The fundi were normal.

Roentgenographic examination showed a debrided defect measuring 3.5 by 5.5 cm in the superior right occipitoparietal region with radiating linear fracture lines

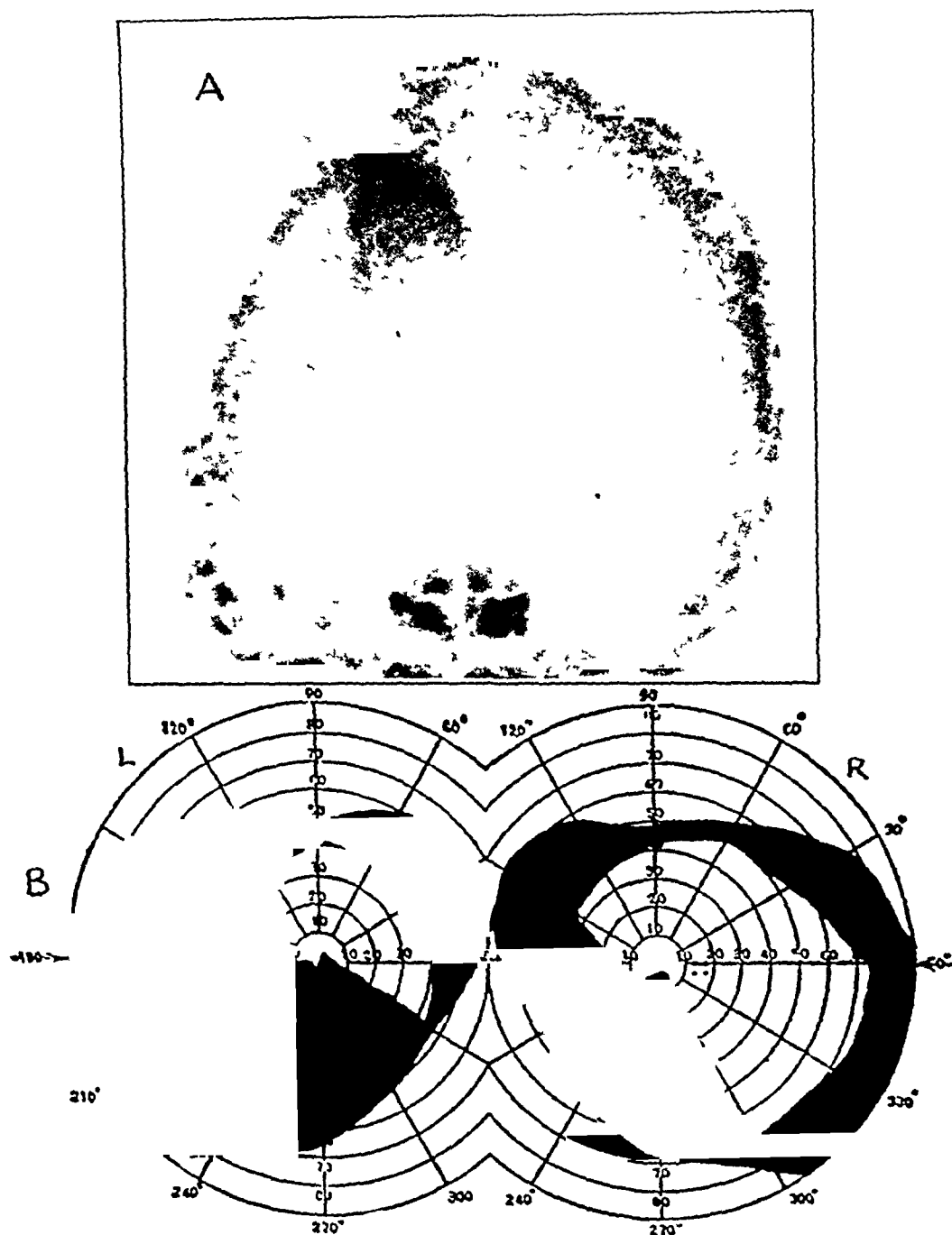


Fig 4—A, roentgenogram, B, visual fields taken Dec 18, 1944 with a 5 mm white test object. Visual acuity: right eye, 12/200, left eye, 2/200.

extending into the left and right lower occipital areas, into the right upper parietal area and along the lateral portion of the right parietal bone into the right temporal bone. Some partially detached fragments of bone lay in the left lateral portion of the bony defect. No intracranial foreign bodies were noted. The optic foramina showed no abnormality.

The field defect was left homonymous hemianopsia with considerable loss of the right lower quadrant of the field of each eye, especially in the left eye, and involvement of both fixation areas

Visual acuity was 20/200 in the right eye and 6/200 in the left eye (eccentric), with ability to read Jaeger type 0

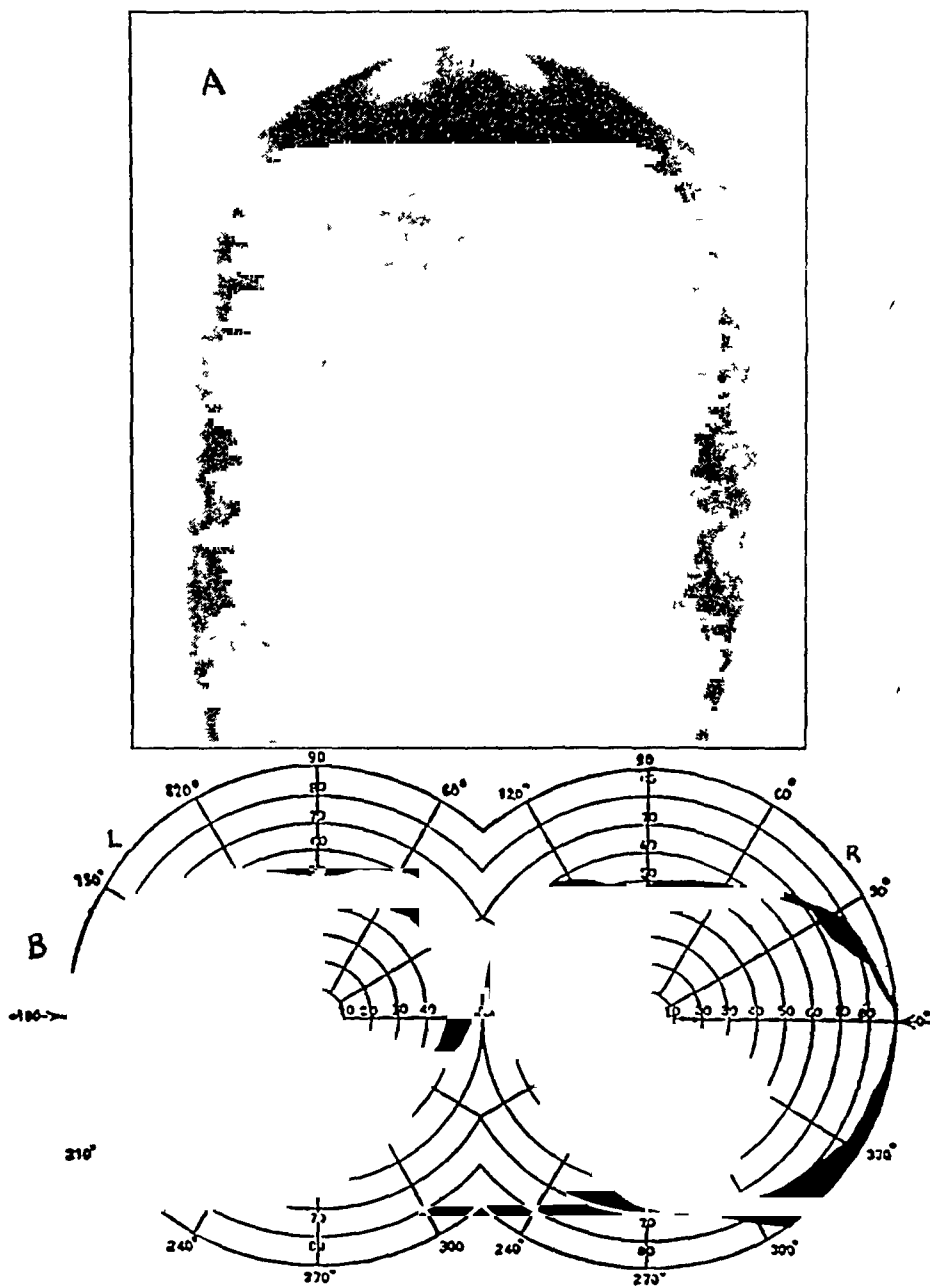


Fig 5—A, roentgenogram, B, visual fields taken with a 3 mm white test object Visual acuity 8/200 in each eye

*Interpretation*—The site of injury and the data obtained at operation and by roentgenographic examination, together with the field defects,

indicate damage to the posterior pole of both occipital lobes, especially the right, and to the optic radiations on the left. The fields varied somewhat between December 18 and January 8.

CASE 5—A white man aged 31 was wounded Aug. 8, 1944 by fragments of mortar shell, sustaining a compound, comminuted fracture of the occipital bone, more extensive to the right side of the midline, with depressed fragments of bone damaging the right occipital lobe.

Two days later craniotomy was performed. The tip of the occipital lobe and the calcarine area on the right side was reduced to pulp by deeply in-driven fragments of bone. The dura was torn on both sides of the midline. The longitudinal sinus was lacerated and thrombosed. Fragments of bone and pulped brain tissue were removed. The soldier was unconscious about eleven days.

Examination showed that he was completely blind for several days after this and later showed ability to count fingers and left homonymous hemianopsia on the confrontation test. The fundi were normal.

Roentgenographic examination showed an irregular defect measuring  $1\frac{3}{4}$  by  $2\frac{1}{2}$  inches (4.5 by 6 cm) involving the occipital bone on each side of the midline, with a stellate fracture extending through the right parietal bone and terminating in the right frontal bone.

The field defect was left homonymous hemianopsia with involvement of both fixation areas and loss of a large portion of the right lower quadrant of the field.

Vision was limited to counting of fingers at 3 feet (90 cm) in the right eye and at 4 feet (120 cm) in the left eye. He read Jaeger type 0 with each eye.

*Interpretation*—The left homonymous hemianopsia was due to damage to the right calcarine area. The damaged area in the left occipital cortex must have lain above the calcarine fissure and involved the tip of the posterior pole to produce a lower field defect with loss of the fixation area.

CASE 6—A white man aged 19 was wounded by a sniper's bullet May 18, 1943, sustaining a gutter type of wound 1 by 3 inches (2.5 by 7.5 cm) in size in the posterior portion of the parietal bones and the superior portion of the occipital bone, chiefly to the left of the midline, with in-driven fragments of bone. Brain tissue was herniated through an infected wound, through which cerebrospinal fluid was draining. Closure of the scalp wound could not be done until June 16, when pinch grafts were used to cover the defect, after the infection had been controlled. Pupillary reaction to light was normal. The fundi were normal.

A roentgenographic examination revealed a gross defect involving the posterior aspect of both parietal bones and the superior portion of the occipital bone, with metallic foreign bodies and fragments of dead bone lying in the brain substance.

The fracture lay chiefly to the left of the midline, with a linear fracture extending into the left parietal bone.

The field defect was complete right homonymous hemianopsia with loss of about one-half the lower left field of each eye and involvement of both fixation areas. There was also loss of the temporal periphery of the temporal field in the left eye.

Vision was limited to perception of hand movements in the nasal quadrants of the right eye and in the temporal quadrants of the left eye.



*Interpretation*—The location of the defect in the skull and the field defect indicate damage to the left occipital cortex with less extensive damage to the right cortex at the posterior pole and above the level of the calcarine fissure, producing the defect in the left lower fields and involvement of the fixation areas

CASE 7—A white man aged 26 was wounded April 29, 1944 by shell fragments, sustaining a compound, comminuted fracture of the right parietal region,

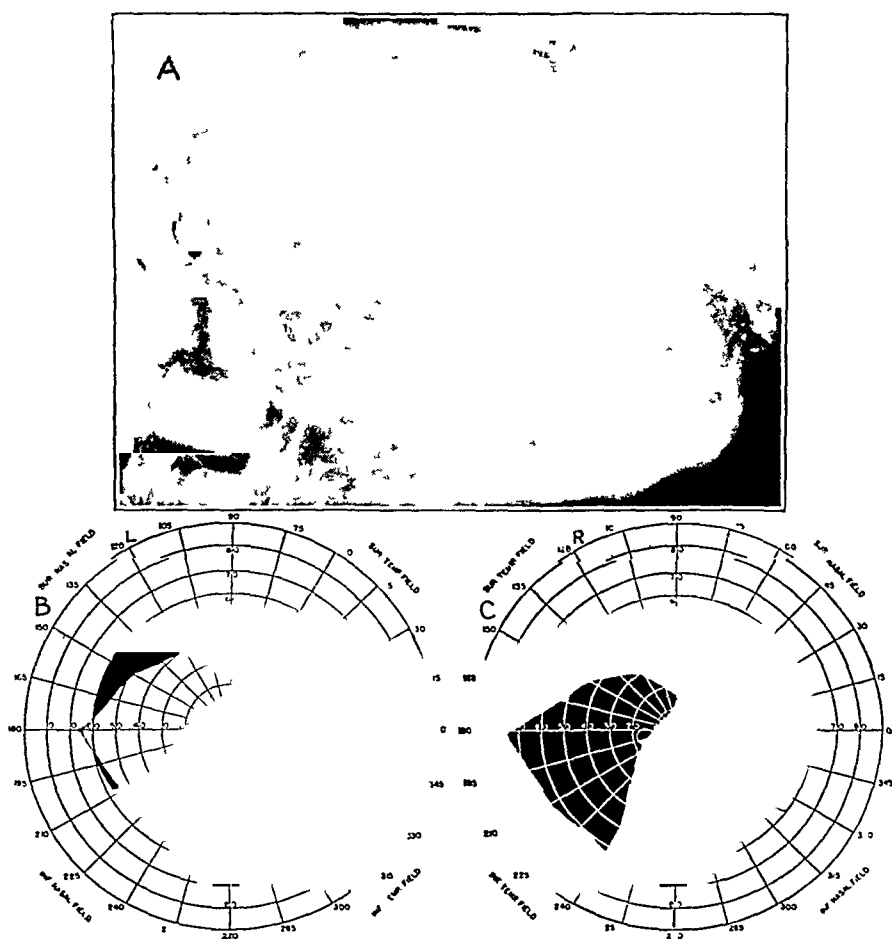


Fig 6—*A*, roentgenogram, *B* and *C*, visual fields of the right and left eyes, respectively, taken Jan 8, 1944 with a 15 mm test object. Vision was limited to light perception in each eye.

with herniation of brain substance from the wound. The patient was totally irrational and had complete flaccid left hemiplegia.

The following day a craniotomy was performed. Devitalized brain tissue was debrided, and the wounds were closed primarily. This had to be repeated seven days later, owing to a new herniation of brain tissue. A third craniotomy was performed because of a deep-seated abscess in the posterior parietal area. After this the patient showed notable improvement and became rational and

cooperative for the first time. Massive intraocular hemorrhages, without evidence of direct trauma to the eyes, had been noted. The patient was said to be entirely blind. He showed pronounced variations in mood.

Roentgenographic examination showed an area of bony dehiscence in the mid-portion of the right parietal bone adjacent to the sagittal suture and measuring

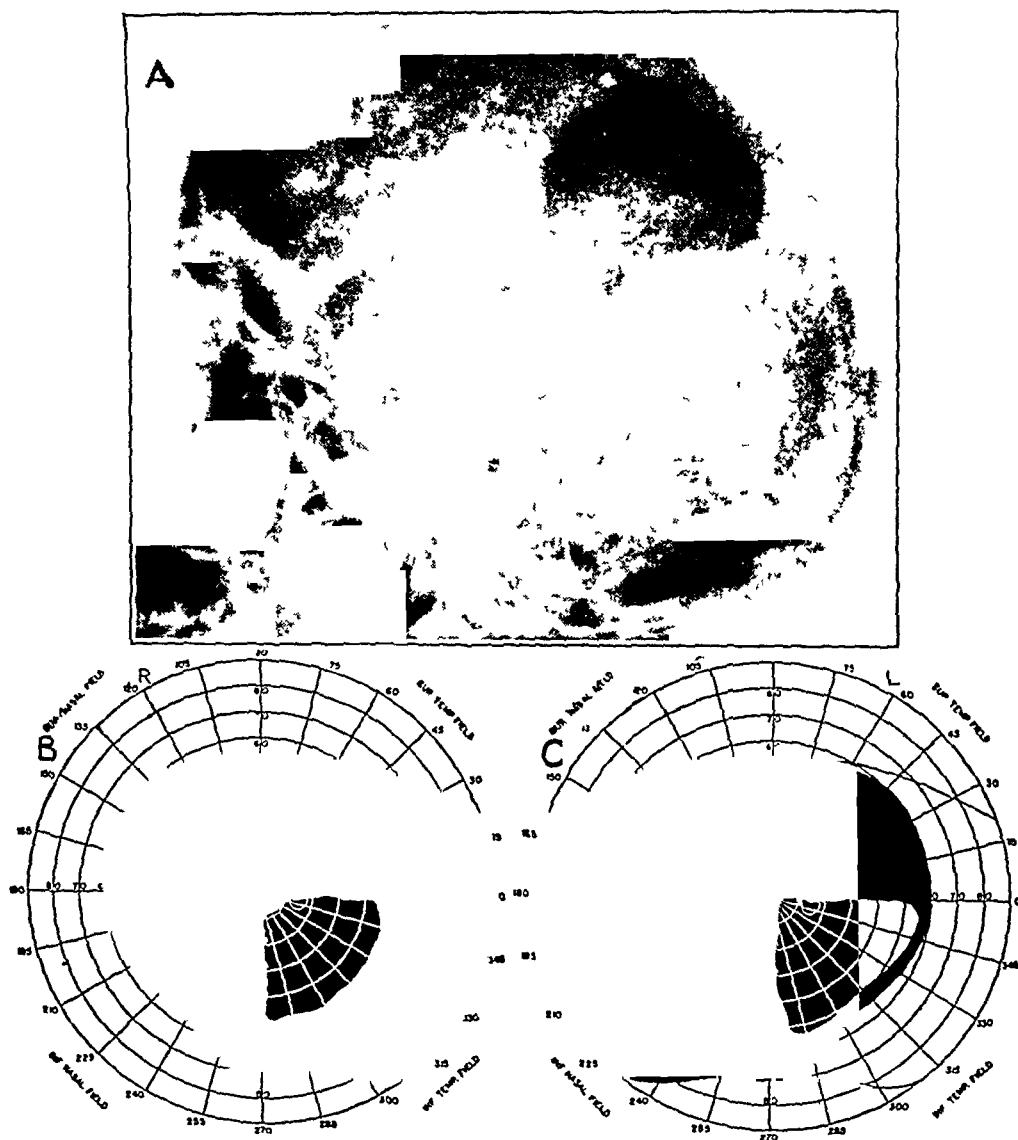


Fig 7—A, roentgenogram, B and C, visual fields of right and left eyes, respectively, taken Oct 28, 1944 with an ophthalmoscopic bulb test object. Vision was limited to perception of hand movements at 1 foot (30 cm).

6 cm in diameter. Two linear depressed fractures extended downward and upward from this defect into the base of the skull.

The field defect was loss of all but a portion of the right lower fields of vision, with loss of both fixation areas.

Vision was limited to perception of hand movements at 1 foot (30 cm) in each eye.

*Interpretation*—Bilateral injury to the occipital lobe, greater on the right side, with damage above the level of the calcarine fissure.

would explain the field defect. Observations at operation did not include examination of the occipital lobes.

A diagnosis of penetrating wound of the right frontoparietal region with a tract of numerous small metallic foreign bodies extending from this area through the right parietal lobe into the left occipital lobe was made overseas. Only widespread injury to the right optic radiations (including the macular fibers) and damage to the left occipital lobe can explain the defect on this basis, and there is lacking sufficient evidence in the record to justify such a statement.

A contrecoup injury to both occipital lobes is a possibility.

The hemorrhages in the vitreous without evidence of direct injury to the eyes may be explained by sudden increase in intracranial pressure with consequent pressure on the vaginal sheath of both optic nerves and hemorrhage from the central vein.

CASE 8—A white man aged 34 was wounded March 25, 1944 by fragments of artillery shell, sustaining an H-shaped, compound, comminuted, depressed fracture of the skull in the midoccipital region just above the lambdoid suture and several deeply placed metallic foreign bodies. Four were near the midline, and one was in the right occipital lobe.

Craniotomy was performed on the day of injury. A laceration of the dura of 2 cm over the right occipital lobe with a tract extending 6 cm anterolaterally into the occipital lobe was found. The tract was debrided and a foreign body removed from the end of the tract with a magnet. A depressed fragment of bone measuring 3 cm was removed, revealing a laceration of the superior longitudinal sinus.

The patient was at first conscious, rational and oriented. He complained of complete blindness. The pupillary reactions and extraocular muscles were normal. On May 28 there developed stertorous breathing and loss of all muscle tone. Lumbar puncture revealed fresh bloody fluid under increased pressure. The patient gradually improved. On April 12 ventriculographic examination was performed, bilateral trephine openings being made in the posterior parietal region. The lateral ventricles were dilated, and there was asymmetry of the occipital horns, the left failing to fill with air. On April 17 a second craniotomy was done. Debridement of necrotic tissue left a cavity 5 by 3 cm in size. When the right ventricle was punctured, the brain began to pulsate for the first time. A second tract was found running parallel to the right occipital horn, 1.5 cm wide and about 8 cm deep. It was felt that a hemorrhage had occurred into the ventricle and that this accounted for damage to the third nerve at the aqueduct.

Roentgenographic examination showed a large, irregular defect in the midline of the skull, involving the superior portion of the occipital and the posterior portion of the parietal bone. A small metallic foreign body lay 2 cm to the right of the midline, deep to the superior border of the defect. The optic foramina showed no evidence of fracture.

The field defect was loss of all the field of each eye except for retention of 2 degrees in each fixation area. Vision was nil for a long time after injury. On June 18 it was unimproved and was limited to light perception in each eye. He read Jaeger type 0 with the right eye and Jaeger type 3 with the left eye.

On Jan 18, 1945 vision had improved to 20/50 +1 in the right eye and to 20/20 —2 in the left eye. He read Jaeger type 2 with each eye, with correction for the left eye

*Interpretation*—Bilateral homonymous hemianopsia with sparing of both fixation areas indicated a lesion in both occipital lobes without destruction of the tip of either occipital lobe, where macular vision is represented in the cortex. This case is the antithesis of case 11 (J H), in which bilateral central scotomas with normal peripheral fields were

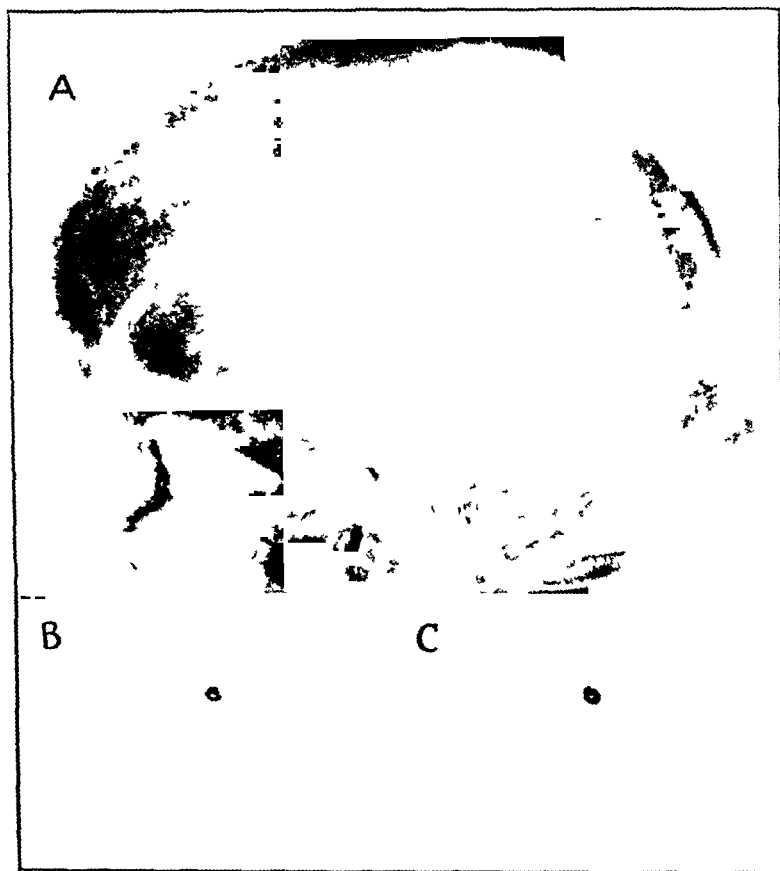


Fig 8—A, roentgenogram, B and C, tangent screen charts for right and left eyes, respectively, taken with 3 mm white test object at distance of 60 inches (15 meters). Visual acuity right eye, 20/100 +1, corrected to 20/50, with ability to read Jaeger type 2, left eye, 20/30, corrected to 20/20 —1, with ability to read Jaeger type 1

found. The exact extent of damage to the optic radiations could not be told. Improvement in vision is accounted for by subsidence of edema in the occipital areas.

CASE 9—A white man aged 26 was wounded March 4, 1944 by fragments of an artillery shell, sustaining a compound, depressed fracture of the left leaf of the occipital bone and several foreign bodies in the left frontal lobe.

Craniotomy was done on the day of injury. This consisted of débridement of the wound in the left occipital lobe, packing of the longitudinal sinus with muscle tissue and closure, with drain in place.

On March 11 he was found to be completely blind, although both pupils reacted to light. There was bilateral papilledema.

On March 12 a second craniotomy was done, with evacuation of a subdural hematoma which was compressing the left hemisphere about 1.5 cm. The left occipital lobe was badly damaged, and the necrotic tissue was removed. A defect 3 cm deep was left. After this, a clot was removed from over the right occipital lobe, the cortex of which was completely liquefied. The neurosurgeon's operative note states: "There was considerable damage to both occipital lobes, thus accounting for blindness. The damage, however, did not appear to me to destroy the calcarine area completely, and it may be that after edema subsides some vision may return, particularly in the upper fields."

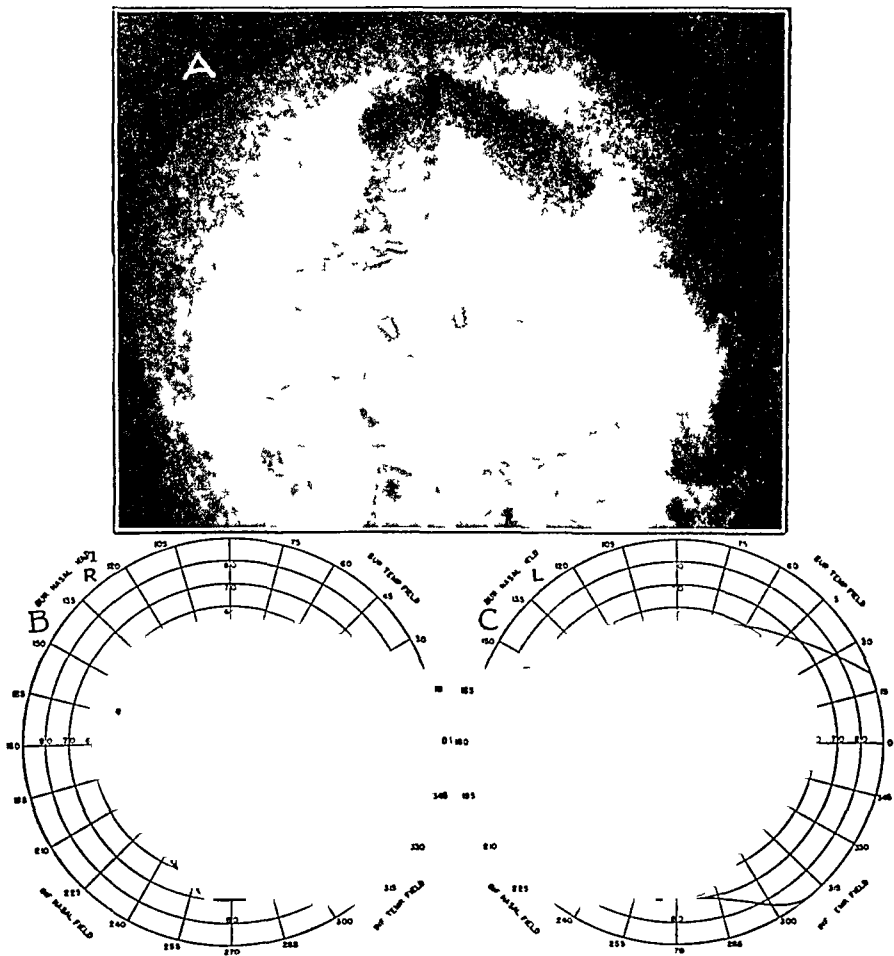


Fig 9—A, roentgenogram, B and C, visual fields of the right and left eyes, respectively, taken Oct 30, 1944, with a 5 mm test object at a distance of 330 mm. Visual acuity 20/40 in the right eye, 20/20 in the left eye.

By March 23 the patient had light perception. When first seen, he could tell time on a wall clock 10 feet (3 meters) away.

On November 16 vision was 20/40 + 1 in the right eye and 20/20 in the left eye, he read Jaeger type 6 with the right eye and Jaeger type 1 with the left eye.

Roentgenographic examination showed a bony defect measuring 6 cm in diameter in the left postparietal area with radiating fracture lines extending anteriorly

The field defect was loss of all field in each eye except for retention of 1 degree in the fixation area. The patient was able to read only one letter at a time, but this he saw quite clearly, both for distance and for near vision

*Interpretation*—There was damage to both occipital lobes, with fortunate sparing of the cortical areas representing the fixation area of the retina. Damage to the anterior portion of the calcarine area accounts for loss of the peripheral field. The fixation area of the cortex of each side must have been preserved. The neurosurgeon felt that the entire cortex had not been destroyed. The radiations are undoubtedly damaged in such injuries as those pointed out by Holmes

CASE 10—A white man aged 23 was injured in a plane crash July 15, 1943, sustaining a compound, depressed fracture in the midoccipital region of the skull with contusion of the right occipital lobe

Thirty-six hours after the injury a craniotomy was performed to elevate the depressed fracture. The edges of the skin were debrided down to the periosteum, two fragments just to the right of the torcula, 3 by 1 cm, found driven inward 1.5 cm and piercing the longitudinal sinus, were pried up and removed. Bleeding was arrested. The right portion of the occipital bone, which had been bent inward, was pried outward. The dura was intact and pulsating freely, it was not opened. The scalp was closed with one layer of interrupted steel sutures. An occipital defect in the skull, about 2 by  $\frac{3}{4}$  inch (5 by 1.9 cm), was repaired with a tantalum plate on Jan 10, 1944

A roentgenogram of the skull revealed a large, irregular defect in the posterior aspect, beginning approximately 4 cm above the lambdoid suture and extending into the occipital bone approximately 4 cm. The defect involved chiefly the right side

The field defect on Aug 13, 1943 was left homonymous hemianopsia with sparing of the fixation area. On Dec 13, 1943 the field defect was left homonymous lower quadrantanopsia with the fixation spared. Vision on the earlier date was 20/30 in each eye, with ability to read Jaeger type 1. On the latter date vision was 20/15 in the right eye and 20/20 in the left eye. He read Jaeger type 1 with each eye

*Interpretation*—The left homonymous hemianopsia is explained by damage to the right occipital cortex

The improvement in the field on second examination, four months later, can be explained on the basis of subsidence of edema in the area adjacent to the destroyed cortex

CASE 11—A white man aged 22 was wounded by fragments of shrapnel March 27, 1943, sustaining injury to the occipital region. Blindness immediately followed the injury. The patient became unconscious about twenty minutes later.

The following day a debridement was performed, and three days later vision began to return. There was gradual improvement in vision until some time in May, after which it remained stationary

On August 2 the depressed fracture of the skull was elevated and numerous bony fragments and pieces of shrapnel were removed. Bony and metallic fragments were removed from the brain tissue in the right occipital pole, and the dura was opened on both sides of the longitudinal sinus. One bony fragment which entered the longitudinal sinus was left in situ, as an attempt to remove it resulted in severe bleeding. Both occipital lobes were found to be grossly

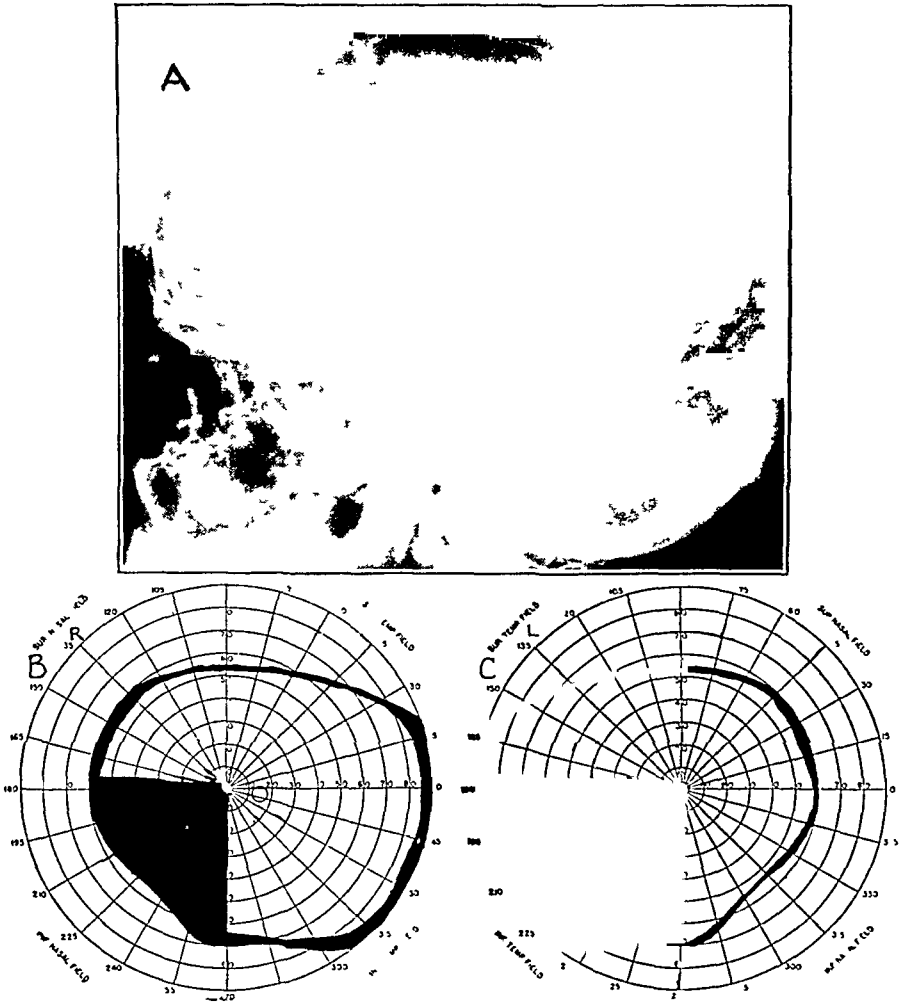


Fig 10—*A*, roentgenogram, *B* and *C*, visual fields of the right and left eyes, respectively, taken Dec 13, 1943, with a 3 mm test object. Visual acuity right eye, 20/15, left eye, 20/20

contused and degenerated, being represented by amorphous xanthomatous scarred cortex. This was freed as well as possible from the dura but appeared to be far beyond any hope of return of function.

On September 24 a tantalum plate was placed in the defect in the skull in the occipital region.

Roentgenographic examination of the skull showed a large defect in the midline of the occipital bone, the lower border being just above theinion. The defect was covered with a metallic plate.

The field defect was a large absolute homonymous hemianoptic scotoma. Vision was 20/200, eccentric, in each eye.

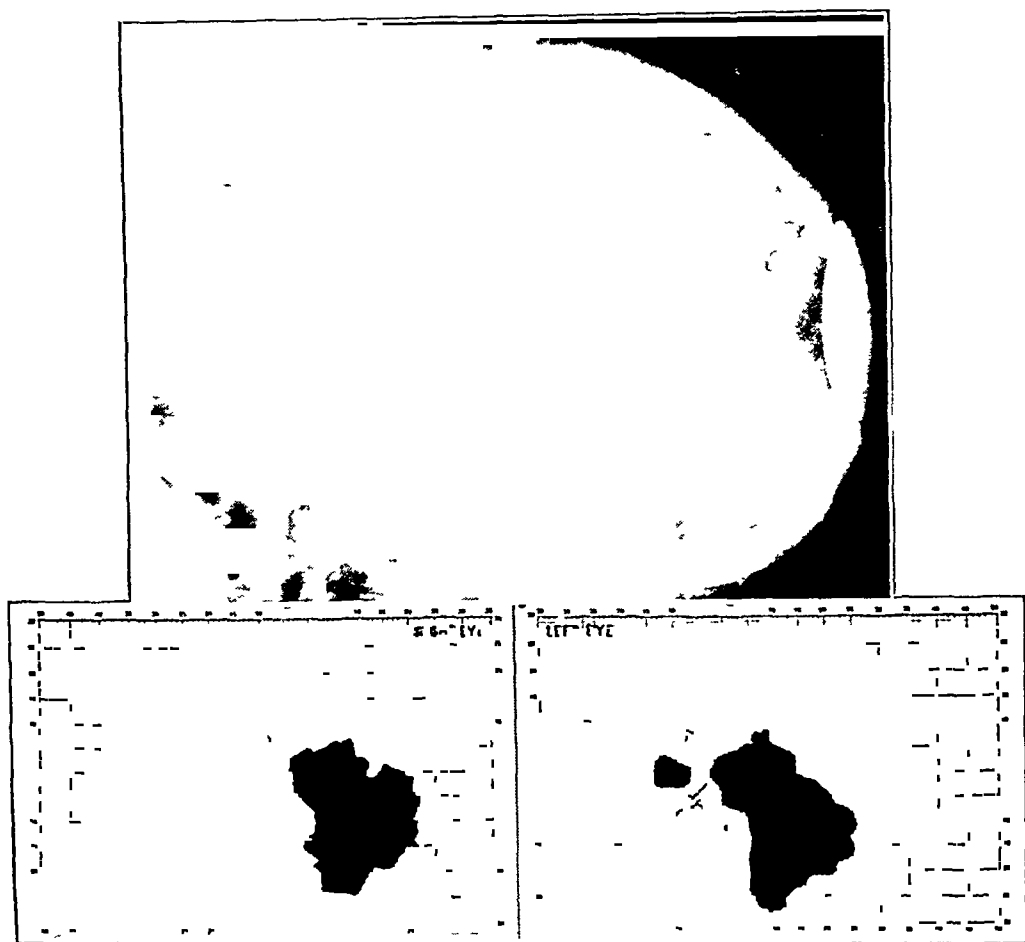


Fig 11—Above, roentgenogram, below, campimetric charts taken Nov 27, 1943, showing absolute scotoma and right homonymous paracentral scotoma.

*Interpretation*—The lesions indicate damage only to the posterior tip of the cortex of each occipital lobe, which was slightly more extensive on the left side.

CASE 12—A white man aged 25 was wounded by an artillery shell fragment March 6, 1944, sustaining a blunt, nonpenetrating blow in the left frontal region.

Two days later it was noted that the right pupil was smaller than the left, both reacted sluggishly to light. Vision was poor in the right eye, and bitemporal hemianopsia was demonstrated. There was paresis of the right sixth nerve. Neurologic examination revealed nothing else of significance.

No operation was performed.

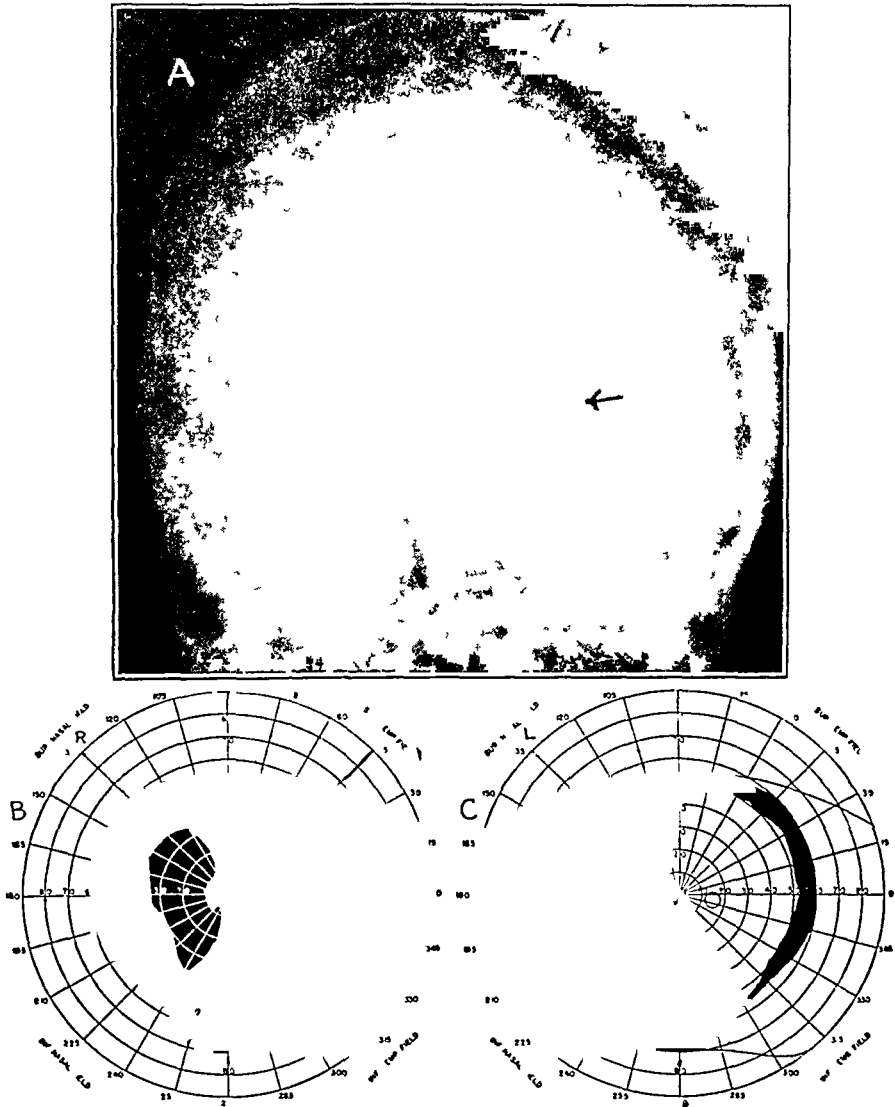
Roentgenographic examination showed a fracture in the left side of the frontal bone, beginning at the superior marginal rim of the orbit and extending upward.



and outward toward the midline. The anterior table of the left frontal sinus was involved.

The fracture extended along the floor of the anterior fossa.

The field defect as noted on May 8, 1944, was a clean-cut bitemporal hemianopsia. On September 10 the right eye showed loss of the entire temporal field, loss of the fixation area and the outer 15 degrees of the nasal periphery. The fixation area was involved. The left eye showed loss of the entire temporal



12—A, roentgenogram, B and C, visual fields of the right and left eyes, respectively, taken with a 15 mm test object on Oct 9, 1944. Visual acuity right eye, 1/200, eccentric; left eye, 20/20.

field except for a small area bordering the midline above the fixation area, which was not involved.

Vision was 1/200 (eccentric) in the right eye and 20/20 in the left eye. He read Jaeger type 0 with the right eye and Jaeger type 1 with the left eye.

The right nerve head was pale, and the lamina cribrosa was clearly seen. The left nerve head showed only a suggestion of pallor. The retinal arterioles were moderately attenuated.

*Interpretation*—The lesion must have been located in the chiasm, involving principally the midportion, with damage to the crossed fibers and sparing of most of the uncrossed fibers. The first field examination showed cleancut bitemporal hemianopsia, but later a defect was found in the peripheral portion of the right nasal field. Vision in the right eye was affected almost immediately after the injury.

In 1935 Traquair, Dott and Russell<sup>13</sup> collected from the literature reports of only 27 cases of lesions of the optic chiasm and added 3 cases. In 2 of these 3 cases the defect was pure bitemporal hemianopsia, in the third case there were blindness in the right eye and a defect involving less than the entire temporal field of the left eye. Even in the first 2 cases central vision was reduced in one eye. Injury was usually to the frontal area and was due to a blunt blow. No fracture was found on roentgenographic examination in 6 cases. The sixth nerve was injured in 7 out of 30 cases. In 7 cases one eye was blind. The olfactory nerve was injured in 5 cases. In 7 cases polyuria was present, although it was transient in 2 cases. Traquair and his associates attributed the chiasmal damage to vascular lesions rather than to sagittal tearing of the chiasm.

Osterberg<sup>14</sup> reported 2 cases, with description of experimental studies on tearing of the chiasm in vitro. He was able to demonstrate multiple small tears and expressed the belief that the blood supply to the center of the chiasm was not separate from the supply to the lateral portions and that therefore the crossed fibers alone would not be affected by damage to blood vessels. Osterberg cited Coppez,<sup>15</sup> who demonstrated multiple minute tears in the crossed fiber bundles. He found that separation of the optic foramina a distance of 12 mm by frontally applied force would produce tears because the optic nerves were firmly adherent to the foramina.

Henderson and Rucker<sup>16</sup> were able to show tearing of the chiasm in 1 case.

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13 Traquair, H. M., Dott, N. M., and Russell, W. R. Traumatic Lesions of the Optic Chiasma, *Brain* **58**:398 (Sept.) 1935.

14 Osterberg, G. Traumatic Bitemporal Hemianopsia, *Acta ophth* **16**:466, 1938.

15 Coppez, H. Le mecanisme des lésions du chiasma dans les fractures du crane, *Arch d'opht* **46**:705-716 (Dec.) 1929.

16 Henderson, J. V., and Rucker, C. W. Bitemporal Hemianopia of Traumatic Origin, *Arch Ophth* **24**:800 (Oct.) 1940.

Burch<sup>17</sup> recorded a case in which a fracture of the sella turcica resulted in bitemporal hemianopsia, vision was 20/25 in the right eye and was limited to ability to count fingers at 6 inches (15 cm) in the left eye

It is evident, therefore, that tearing does occur although damage to the blood supply must be considered as at least a contributory cause

#### CONCLUSIONS

1 Correlation of visual field defects with definitely known sites and types of head injury, the lesions found at operation and the results of roentgenographic examination of the skull offers the best method of studying the cortical representation of various areas of the retina

2 Cortical representation of the fixation area (macula) is similar to cortical representation of the peripheral portions of the retina. The fixation area is represented at the posterior tip of the occipital lobes, while the peripheral portions of the retina are represented in the cortex at the anterior end of the calcarine fissure. Intermediate points of the retina are represented between these two areas of the area striata

3 Similarly, the upper half of the retina is represented in the cortex above the level of the calcarine fissure, while the lower half of the retina is represented below the calcarine fissure

4 Neither the fixation area (macula) nor the peripheral area of the retina has duplicate areas of representation

5 It follows, therefore, that homonymous hemianopsia, vertical hemianopsia and quadrantanopsia can occur in the peripheral field and that the central fields may also show homonymous scotomas, which may be lateral or vertical, central or paracentral, hemianopic or quadrantic. Combinations of homonymous hemianopsia and central scotoma also occur when missiles producing oblique wounds pass through the tip of one occipital lobe and through the occipital lobe or the optic radiations on the opposite side, as shown by Holmes and Lister

6 Bilateral homonymous hemianopsia with sparing of the fixation areas (cases 8 and 9) represents the antithesis of bilateral central scotoma with normal peripheral fields. These cases support some of the statements in previously expressed conclusions

7 Bitemporal hemianopsia can occur from damage to the chiasm, although it is rarely a "pure" hemianopsia. The mechanism of this damage to the uncrossed fibers alone is not entirely clear

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<sup>17</sup> Burch, F. E. Ocular Evidence of Head Trauma, Wisconsin M. J. **41** 1092, 1942

# PLASTIC REPAIR OF DEFORMITIES OF THE SOCKET AND MINOR DEFECTS ABOUT THE ORBIT

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THE ANATOMY of the socket deserves a clearer presentation than the anatomy of this region usually receives. "Socket" means the bed or receptacle of the prosthesis. Theoretically, consideration of the anatomy of the region should be simple, since its spatial relationships have been covered in great detail. Actually, the anatomy, and more particularly the physiology, of the orbit without the eye departs farther from the normal than study of the literature would lead one to think. The ratio of the volume of the globe to that of the orbit, according to Duke-Elder, is 4.5 : 1, but the removal of the one part makes a profound difference in the other.

There are essentially four types of sockets, depending on the procedure or the series of procedures by which the eye is removed. A separate discussion of each type, although elementary, may be advisable.

1. Socket formed by enucleation of the globe without an implant sphere, the procedure consisting of suturing together of the extraocular muscles and Tenon's capsule and covering with conjunctiva. This operation is the simplest and gives a fairly satisfactory base for a prosthesis. Movement is generally adequate, the method giving approximately a 10 degree range of movement of the prosthesis vertically and horizontally. Its principal disadvantage is that alteration in function causes atrophy of the orbital contents, which results in poor movement of the prosthesis. This point will be discussed later.

2. Socket formed by enucleation of the globe with an implant sphere placed in the cavity created by removal of the globe. Retention is obtained by suturing Tenon's capsule and the muscles together and covering with conjunctiva. The implant sphere may consist of any acceptable material—glass, tantalum, gold, plastic or preserved cartilage. We have had several bad results with implant spheres of bone, which have had a tendency to undergo necrosis, resulting in a foul orbital discharge and necessitating removal of the implant, with almost no hope of implanting another sphere because of the large amount of scar and fibrous tissue which forms around the bone in this area. This type of

socket gives better movement of the prosthesis than does the type previously discussed. The size of the implant should approximate the normal to give the best movement. If the implant sphere is too small, the purpose to give better mobility of the prosthesis will be defeated, and the implant will be no better than none at all. If it is too large, fitting an acceptable prosthesis is difficult, and Tenon's capsule may slip back from the sphere, leaving it thinly covered and vulnerable. Thus, the preparation of this type of socket in children is a poor choice, because the sphere is necessarily of limited size and in later years it shifts in the socket, making almost impossible the fitting of a prosthesis which is realistic in appearance and movement.

3 Socket formed by evisceration of the global contents, removal of the cornea, closure of the sclera without an implant and coverage with conjunctiva. The surgical indications and contraindications for this procedure are well covered in the literature and have no place in this discussion, which is concerned principally with results. From the point of view of the mobility and appearance of the prosthesis, the socket prepared in this way is much better than the two previously discussed. The prosthesis generally moves better horizontally and vertically, and there is also retained more than a suggestion of the action of the oblique muscles, since they are still intact. In our experience, the sockets which were prepared in this way when the patients were children had better beds for the reception of a good prosthesis in adult life than those formed by enucleation, either with or without implant.

4 Socket formed by evisceration of the ocular contents with an implant sphere placed in the scleral sac, followed by closure of the sclera and conjunctiva. This procedure undoubtedly gave the best results. Movement of the prosthesis was 50 per cent normal or better both vertically and horizontally. The amount of late atrophy was about the same as that in the third type of socket and was much less than with enucleation.

The changes which occur from removal of the eyeball until the death of the patient are fairly progressive and account for the further variety of sockets which we have seen.

The bony walls of the orbit are usually unchanged in the removal of the eye, although when they are altered, as in battle casualties, additional problems are presented. Normally, the lateral wall of the orbit is the strongest, especially where the frontal bone joins the great wing of the sphenoid bone and the zygomatic bone. At this point the margin is curved backward so that the visual field may be wide laterally, and there are almost no structures of the bony walls to interfere with this function. The orbital tubercle is at about the middle of the lateral wall, and to it is attached the lateral retinaculum. From this point up to the

site of insertion of the combined tendon of the superior rectus and the levator palpebrae superioris muscle there is almost no integral attachment between wall and contents, as there is in the other quadrants of the orbit. It is for this reason that no structure holds the implant there. Considerable atrophy of orbital fat is seen to a greater or less degree in all sockets with which we have come in contact, and this apparently was the original experience of Snell, since the prostheses generally have their greatest area in this location. Associated with this atrophy, as with all other changes in the socket, is the factor of gravity. The check ligaments of unused muscles and the muscles themselves become soft and tend to fall to the floor of the orbit when the edema and hemorrhage associated with the operation are absorbed and replaced with fibrous tissue over the years. In most sockets which we have examined fifteen or twenty years after the operation there is a redundant mass of tissue at the floor of the orbit, making the fitting of a prosthesis which is lifelike a difficult task.

Associated with the alteration in function in the socket, various changes occur in the conjunctiva. These changes begin almost as soon as removal of the eye is finished and are usually more profound than is generally indicated. For example, in a case of evisceration in which the cornea is removed, the loss of tissue, necessitating coverage by the conjunctiva, is usually compensated for by decrease in size of the globe. Normally the conjunctiva is more than ample and folds into the fornices. However, when the associated edema and hemorrhage have subsided, the conjunctiva loses its normal elasticity by replacement of elastic fibers with fibrous tissue. It becomes thickened and resistant, like a rubber band which after being on stretch is suddenly relaxed. This change occurs in the orbital, fornical, bulbar and limbal conjunctival areas. The changes are modified somewhat by the type of operation and by the length of time that elapses between the operation and the insertion of a conformer or prosthesis. We have seen a number of cases in which the time which elapsed after operation was as long as twenty years. In such cases the conjunctiva is firm and fibrous and the lower fornix, or sulcus, is entirely absent, so that one of the separative procedures must be carried out.

Grossly, the conjunctiva of the eye is considered as consisting of four portions. The palpebral portion, made up of marginal, tarsal and orbital conjunctiva, the conjunctiva of the fornix, the bulbar portion, consisting of scleral and limbal conjunctiva, and the plica semilunaris. Microscopically, the conjunctiva is made up of an epithelial layer and a substantia propria, consisting of an adenoid and a fibrous layer. The deeper, fibrous, layer is a thick collection of collagenous and elastic fibers. It is absent over the tarsal region but begins at the edge of the tarsus and extends back over the orbital portion of the conjunctiva of

the globe. It is reenforced by the insertion of the levator in the upper fornix, and we feel that this reenforcement is the reason that fewer changes are seen in the upper portion after operation. The change takes place in the substantia propria of the conjunctiva, most likely in the elastic fibers of the fibrous layer.

Within the upper lid are two potential spaces, separated by the aponeurosis of the levator muscle. Both these spaces are lost and the lids are profoundly involved in the metamorphosis of the structures. The changes in the eyelids are much greater on their external surfaces. The superior orbitopalpebral sulcus is deepened, and the inferior orbitopalpebral sulcus tends to be obliterated. The fornices, as we have noted before, are lost, and the fibers of the orbicularis muscle become relaxed and redundant. This is especially true inferiorly. One of the operations to be described later is helpful in repair of this condition. The elasticity of the lids is not lost to the extent that it is in the conjunctiva, and the changes seem largely innervational, or trophic. It is felt that the change is in the septum orbitale, since the most profound effect is in the lower lid, where this septum is complete. In the upper lid, where the septum blends with the levator muscle, the changes are not so pronounced.

To summarize. It is felt that after removal of the visual mechanism there are certain uniform changes in the eyelids, muscles, conjunctiva and socket which are in the nature of atrophy, that these changes proceed along fairly uniform lines, although their progression may be altered substantially by early and well fitting prostheses, and that once they are well established the only effective treatment is with the operative procedures to be discussed.

#### OPERATIVE PROCEDURES

Various modifications of procedures for correction of contracted socket with free skin grafts have been presented in the literature.<sup>1</sup> Wheeler<sup>2</sup> has practically standardized the technic of operation, but a few problems encountered in large scale repair at ophthalmic centers should, we feel, be taken into consideration when deviations from standardized procedures become necessary.

We do not believe that Wheeler and others intended to standardize a procedure which was to be used in every case of contracted socket.

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1 Kilner, T. P. The Application of the Thiersch Graft to Special Areas, *Post-Grad. M. J.* **10** 317, 1934. Spaeth, E. B. Principles and Practice of Ophthalmic Surgery, ed. 2, Philadelphia, Lea & Febiger, 1941. Sheehan, J. E. Plastic Surgery of the Orbit, New York, The Macmillan Company, 1927.

2 Wheeler, J. M., cited by Spaeth, E. B. A Review of Some Modern Methods for Ophthalmic Plastic Surgery, *Am. J. Surg.* **42** 89, 1938. Use of Epidermic Graft in Plastic Eye Surgery, *Internat. Clin.* **3** 292, 1922.

There are many variations in deformities of the socket, and these should receive much more consideration than they have in the past and their repair planned accordingly. The terms "never" and "always" should not apply in this type of reconstruction, since so much good is done by procedures which may have been condemned by some surgeons but have served a good purpose in the hands of others. Repair of the socket, in our opinion, deserves as much consideration as any other form of repair about the orbit and face. On a well planned repair will depend the

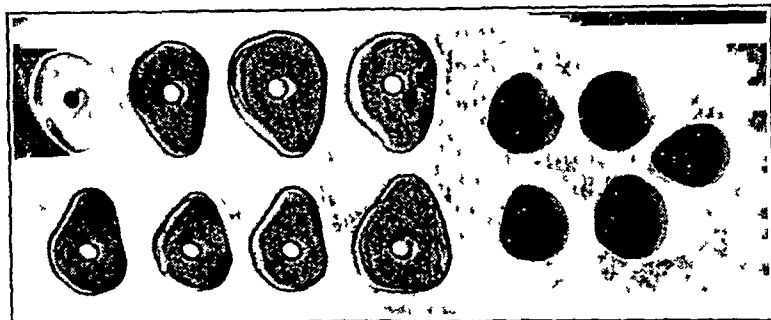


Fig 1—Different types of acrylic conformers used in eye sockets after various grafting procedures, as illustrated in the text. The clear acrylic type is usually inserted after the stent or rubber mold is removed. The others were made according to the size and shape of artificial eyes. Lately we have substituted clear acrylic plugs.



Fig 2—*A*, socket completely lined with skin. Notice the remnant of caruncle preserved. There is also a deformity of the left eyebrow, which was corrected by the Z plastic operation, as seen in *B* (operation performed with Major Sanders K Stroud). *B*, result after insertion of artificial eye and correction of the deformity of the eyebrow.

satisfactory fitting of a prosthesis. In these circumstances, there cannot be a standardized method of repair.

With the advent of acrylic artificial eyes, patients are becoming much more eye conscious and are as much disturbed with a slight exophthalmos as with the notching of the lids or a misplaced eyebrow. This is just an example of what ophthalmic surgeons can expect on return to



civilian life, and they must be prepared to analyze the various contours of the orbit and to plan operative procedures accordingly, in order better to assist in the fitting of a prosthesis that will satisfy the patient

*Complete Lining of Socket with Skin*—We agree that there is little difficulty in the method of completely lining the socket with skin. When we consider the factor of movement, we are inclined to work out a definite plan for this procedure. Every patient desires as much movement as possible in the prosthesis. A completely skin-lined socket has a tendency to restrict movement in many cases, and in a socket requiring a complete lining, including both cul-de-sacs and the lids, we suggest grafting the lids and both cul-de-sacs first and leaving the central, movable, portion of the socket for a second stage procedure. We found that a line of demarcation at the junction of the movable-nonmovable portions of the socket adds greatly to the final movability of the fundus of the socket. This was brought to our attention in the repair of pre-



Fig. 3—Result of lining the lids and the nonmovable portion of the socket with skin. The old graft in the central portion of the fundus was not disturbed. The central, movable, portion of the socket has the appearance of having a fat graft implanted. Notice the depth of both the superior and the inferior cul-de-sac.

viously grafted sockets with absence of both cul-de-sacs. The graft in the central portion of the socket was left intact, and movement was decidedly increased. The contour of the socket was also greatly improved, and the fundus had the appearance and consistency of a previously inserted fat graft or other implant. We have found in the case of the greatly retracted socket that a flap for the central portion might be more desirable because of the frequent necessity of secondary incision and implantation of some material. In our series of complete linings no flap was necessary.

Dental stent has been a favorite material for the grafting of these sockets, but to make a complete and satisfactory lining with stent a canthotomy is often necessary. Personally, we do not feel, as do some surgeons, that performing a canthotomy is malpractice, since it can easily

be repaired. However, in consideration of the principle of not producing any more incisions than necessary, we have adopted the use of the rubber pad, as illustrated by Hughes and others, thus producing contact with all surfaces without any widening of the palpebral fissure. The pad is readily inserted with the graft and readily removed. Latex pads are ideal, provided they have a flat and slightly concave surface posteriorly and a slight convexity anteriorly. Frequently a pad with more convexity posteriorly is indicated, since it will produce more pressure against the posterior portion of the socket to be lined. Ordinarily, orthopedic rubber padding is rather firm but serves the purpose when shaped properly. A hole is placed in the central portion for drainage.

*Absence of Conjunctiva*—All scar tissue on the lids and in both cul-de-sacs and in the socket itself is excised. Thin lids are essential, and the tarsus of the lower lid should be hugged in the dissection. If possible, the dissection should be begun slightly below the margin of the lid, it is continued inferiorly along the floor of the orbit, externally beneath the skin to the lateral orbital rim and medially to the margin of the lacrimomaxillary junction, care being taken to stay behind the caruncle or the remnant of the caruncle. Any remaining tissue should be retained in this region so as at least to simulate a caruncle. A portion of scar tissue is better than nothing at all, from the standpoint both of the cosmetic effect and the fitting. One can do tattooing later, if necessary, and dissection is then continued superoposteriorly, care being taken to avoid the fibers of the levator palpebrae superioris. Inferiorly, laterally and medially the periosteum should be roughened or incised so that the graft will become readily adherent in these regions. The rubber pad is then shaped accordingly and inserted, care being taken that there is contact all around. If a stent mold is used, hot or cold, sterile water should be available, a canthotomy performed and the mold shaped accordingly. The inner side of the upper portion of the arm is usually the choice for the donor area. A thin split graft is removed from this region and applied on a wet towel, with the raw surface down. Petrolatum gauze, gauze soaked with saline solution and a cotton wool dressing are applied over the donor area. The previously prepared mold is then placed on the graft and the graft applied over the mold. Glue is not necessary, and in our experience a thin graft is desirable. This graft is punctured in the central portion so as to provide for drainage through the hole in the mold. The mold and the graft are then inserted into the socket, with the raw surface of the graft on the outside. The lids are then approximated with two silk sutures, petrolatum gauze strips are applied, with an eye pad and fluff gauze pressure dressing. The lid sutures are removed on the fifth day, the mold is removed on the seventh day, and the socket is flushed with boric acid. The mold is then reinserted. On

the ninth day the mold is removed and an acrylic form inserted, as illustrated (fig 1) This acrylic form is fitted accordingly and has a hole in its center for irrigation and drainage This form can be removed at weekly intervals for cleansing and should then be reinserted until the contracture period of the graft has passed, which is usually from six weeks to three months A form in the shape of an artificial eye can then be inserted and worn for a time, while the patient awaits the fitting of a satisfactory prosthesis The graft within the socket is important and should be cleansed daily, followed by the application of a lubricant One should not be in too great a rush to insert a permanent prosthesis but should wait until the graft has softened and has approached maximum contraction

In the two stage procedure, the same technic is followed, and the central portion is grafted as a separate entity We suggest suturing the graft in place, with the ends left long, so that they can be tied over

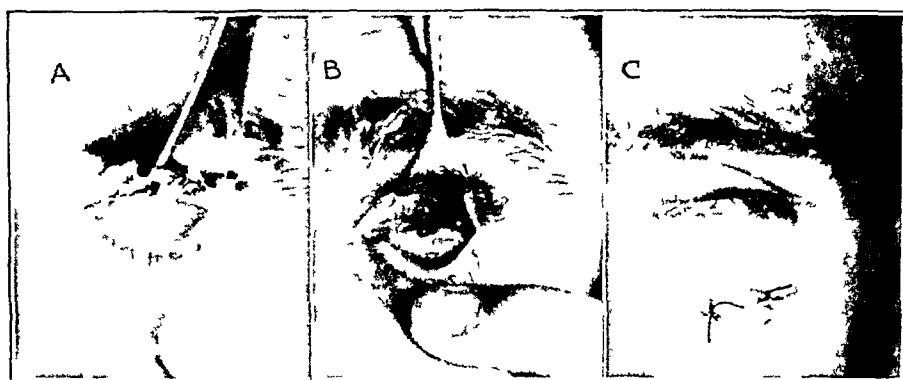


Fig 4—*A*, absence of the inferior cul-de-sac The socket could not retain the artificial eye The procedure outlined in the text was performed with a mucous membrane graft from the lower lip *B*, result of procedure A satisfactory cul-de-sac was produced *C*, sutures tied over a piece of gauze on the cheek after insertion of a mucous membrane graft, as described in the text A photograph of a different patient had to be shown for illustrative purposes, the sutures in the case shown in *A* and *B* having been removed before a photograph was available

a fitted mold to provide pressure on the graft Fluff gauze can be used for this purpose instead of a form-fitting mold

*Absence of the Inferior Cul-de-Sac*—This condition may be caused by lack of sufficient conjunctiva, cicatricial deformity or overabundance of conjunctiva, with the result that the artificial eye cannot rest properly and persists in slipping out In cases of insufficient conjunctiva the mucous membrane graft is indicated With local anesthesia, the socket-lid junction is determined and an incision made along this line All scar tissue is excised The incision is then extended down to the orbital floor, and care is taken to release all adhesions and attachments Medially, the incision is extended in an oblique direction, to pass

laterally and beneath the caruncle. Laterally, it is extended to a few millimeters above the external canthus, assuming the appearance of a hammock. A small gauze strip is inserted to control bleeding. The inside of the lower lip is an ideal donor area. Sutures are inserted in the lower lip for traction purposes. With local anesthesia, the mucous membrane is ballooned out, and a full thickness graft is outlined and excised. The resulting raw area is repaired by direct approximation with a continuous suture of silk and interrupted sutures of silk. The graft is then transferred to the raw area of the cul-de-sac and sutured in place with fine silk. Interrupted sutures, with the ends left long, are inserted at intervals. The most important part of this procedure is the insertion medially and laterally of a stay suture of silk, entering through the graft and passing through the periosteum of the infraorbital rim and then out through the cheek. A piece of petrolatum gauze is placed within the socket between the loops of the sutures on top of the graft and the ends tied without over a piece of petrolatum gauze. This procedure assures one of a permanent sulcus because of the attachment of the graft to the floor of the orbit, and without this attachment the operation must be considered unsuccessful. The previously inserted interrupted sutures at the graft-conjunctiva junction are then tied together over the petrolatum gauze within. An additional petrolatum gauze pack is inserted into the socket, and the lids are sewed together with two interrupted sutures of silk. Petrolatum gauze, an eye pad and fluff gauze pressure dressing are applied.

A piece of stent, latex or sponge rubber may be used instead of the petrolatum gauze, but this is not necessary. We have sutured the graft to a latex or sponge rubber prefitted mold and inserted this mold and graft over the raw surface, but our results have not been as gratifying as with direct suture. The cheek sutures are cut the fifth day but not removed. The lid sutures are cut the seventh day. The petrolatum gauze pack is removed the ninth day, together with all the sutures, and an acrylic conformer corresponding to the shape of an artificial eye is inserted, as seen in figure 4. A certain amount of conjunctivitis will result, together with some purulent drainage. This is controlled by repeated irrigations with boric acid or some other appropriate solution. We do not wait for contraction in these cases, but the patient is fitted as soon as the socket and adjacent lid have assumed their normal appearance and all conjunctivitis and swelling have subsided.

*Absence of Cul-de-Sac Due to Redundancy of Mucous Membrane* — Frequently there is absence of the cul-de-sac, and examination reveals a redundancy of conjunctiva, producing a direct continuity between the margin of the eyelid and the socket. An attempt should nevertheless be made to fit a prosthesis in a case of this type, since if the exertion of force from the upper lid or the region of the upper cul-de-sac is properly

directed and a satisfactory socket is made available it is possible that the artificial eye can be fitted and the redundant mucous membrane depressed, with the cul-de-sac assuming a normal appearance. If the artificial eye is not retained, there may be a notch available in the socket by which an appliance can be attached to the artificial eye and held by the notch. Frequently, however, regardless of what attachment is made to the artificial eye, the eye must be extremely thin and of the shell type, and it will inevitably rest on the lid rather than the sulcus or the bed prepared for it. In these circumstances, it is far more desirable to incise the conjunctiva along the inside approximately at the line of the lid-socket junction, extend the incision to the floor of the orbit, roughen or incise the periosteum, invert the edges of the conjunctiva and attach both flaps to the periosteum of the anterior portion of the rim. The same type of suture is inserted as is used in making a mucous membrane graft, only both edges of the conjunctiva are incorporated in the suture that passes through the cheek. We suggest a central point of anchorage, as well as the two lateral points. In these circumstances, a desirable sulcus will be produced. Care must be taken to leave the anterior flap of conjunctiva long enough that the lid will not be inverted and depressed after anchorage. A suture passed through the conjunctiva and anchored without incision is not sufficient. Raw edges must be produced and a new line of cleavage established.

*Skin-Mucous Membrane Combination*—The combination of skin and mucous membrane as a lining for the lids and socket has been condemned by many excellent clinicians. On the other hand, it has been, and still is, used by many without any untoward effect. We see no contraindication whatever to combining the two. Battle casualties present an entirely different pathologic problem in repair. We have had cases in which we completely excised the scar tissue and inserted a mucous membrane graft, and within a few weeks the only remnant of the graft was a ball of mucous membrane incorporated in more scar tissue. Secondary repair with implantation of a thin split graft relieved the situation and gave us an excellent result. Our method of choice is always use of mucous membrane, but in extensive deformity due to scar tissue, especially in the upper cul-de-sac, and secondary contractures following mucous membrane grafts in the presence of healthy conjunctiva elsewhere within the socket or lids, we see no contraindication to use of this combination. We agree that the secretions are increased greatly for a period and desquamation exists for a time, but this condition is gradually reduced to such an extent that ordinary mechanical cleansing of the socket will relieve the situation.

Within three months to a year the graft becomes soft and flexible and is easily displaced by a prosthesis. Except for its appearance, it assumes all the characteristics of the host. In lining both lids with

skin, we still attempt to retain the central portion of the conjunctiva, provided it has a normal appearance. If the excision of the central portion is necessary, it can be done at a later stage.

Whatever procedure is employed, we cannot stress too strongly the importance of building sulci sufficiently deep, since the depth is more easily reduced by excision of the graft than increased by the addition

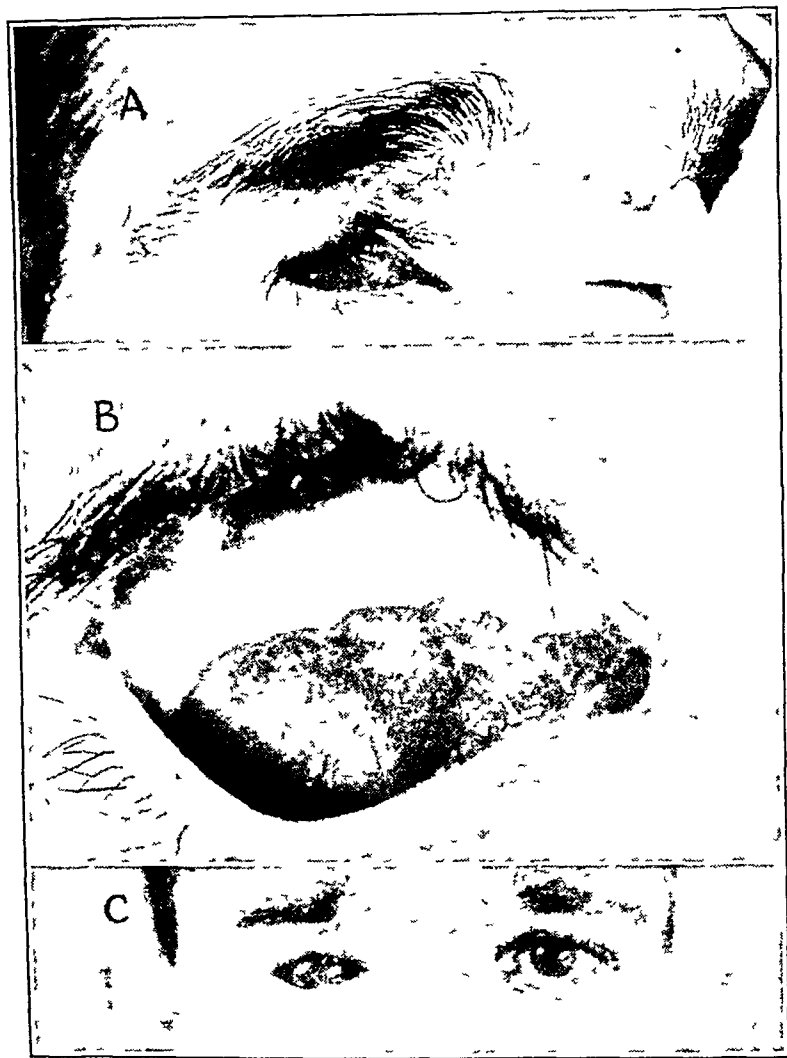


Fig 5—*A*, condition of the right orbital region on the patient's admission. The upper lid was adherent to the socket. Implantation of a mucous membrane graft was attempted in the superior cul-de-sac and failed. The "take" was satisfactory, but it shrank to a small area of combined mucous membrane and cicatricial tissue. Previous to this a full thickness graft from behind the ear was placed in the upper lid to lengthen the lid and release the eyebrow, which was lowered, as seen in the photograph.

*B*, the combined skin-mucous membrane graft in the same eye. The remnants of previously inserted mucous membrane and scar tissue were excised, and a thin split graft from the inner side of the arm was inserted. This photograph also shows the result of lengthening the upper lid with a previously applied full thickness graft. The notching was repaired by the Wheeler halving method.

*C*, result of the repair described in *B*. An acrylic plug was inserted and the notching corrected. The socket is ready for insertion of the artificial eye. The patient had a small bony defect beneath the outer portion of the eyebrow. A cartilage graft was contemplated, but release from assignment prevented us from carrying out the procedure.

of more graft Full thickness mucous membrane is employed extensively The thinner the skin graft the better, provided enough support is given to the graft over a sufficiently long period to prevent too much contracture If skin is properly anchored, this does not become a very important factor, except in the superior cul-de-sac, where periosteal anchorage is out of the question For this same reason, the superior cul-de-sac should be of much greater depth in order to compensate for some of its reduction in size by contracture of the graft

Mucous membrane will not contract to the same extent, but still the graft should be wider than the raw area presenting, in order to provide for its anchorage to the orbital floor We have lined both upper and lower cul-de-sacs with a single graft of mucous membrane but have found that the final result is not very satisfactory because of the tendency of the graft to contract in all directions toward the central portion of the socket It is a far better procedure to line both cul-de-sacs with mucous membrane, either at the same time or at a second stage, but to interrupt the continuity of the graft at the medial and lateral canthal regions In these cases we like to extend the graft in the inferior cul-de-sac slightly above both the inner and the outer canthal region

*Complications Existing in Socket Repair* —The caruncle is seen as inevitably attached to the socket and frequently elongated, extending in all directions Without a visible caruncle the eye looks flat and bare at the inner canthus, and every effort should be made to reconstruct one if absent or to attempt to make it available if present The ideal caruncle is one which is not elongated and which is just a soft, fleshy attachment of the socket, so that when the prosthesis is inserted the medial portion falls behind the caruncle in a groove which has all the appearance of having been made to receive the prosthesis Another type is firmly attached to the socket, but there is sufficient resilience in the conjunctiva of the socket that the insertion of the prosthesis will invert the outer portion and the appearance of the medial portion will be satisfactory

Another type of attachment in which we are chiefly interested is the caruncle that is bound down to the orbital socket with scar tissue, either attached firmly all around or in the form of a rigid band If attached firmly, it is split, leaving a medial portion slightly larger than the normal caruncle in the good eye The incision is then extended medially and posteriorly to the lacrimomaxillary junction A mucous membrane graft is then inserted and attached to the periosteum, as described in repair of the inferior cul-de-sac If attached with a scar band and in the presence of normal redundant conjunctiva, a Z plastic operation will serve the purpose, the elongated lateral portion of the caruncle being completely excised up to the required medial por-

tion The choice of procedure should always be that which will simplify the fitting of a prosthesis and retain as normal a relationship as possible between the caruncle and the medial scleral exposure of the artificial eye

It is important to notice the relationship of the caruncle to other structures in the normal eye It is attached superiorly by way of the plica, and also inferiorly, but it likewise assumes an oblique position, and in many cases the apex of the triangle is attached to the lower lid, inferiorly and posteriorly

The eye travels along the caruncle in its inferior medial portion, and an attempt should be made to place the caruncle in this position so that the artificial prosthesis can accommodate itself to as normal a position as possible

*Atony of Lower Lid as a Complication*—This condition is inevitably present in older patients and, we believe, is frequently caused by the wearing of a prosthesis over a long period In the greater percentage of these cases no sulcus is present, or if a sulcus is present it is found near the margin of the lid rather than at the lid-socket junction Even a shell eye worn over a long period will tend to produce an atonic condition of the lower lid, with drooping and slight ectropion To avoid this in future fittings, we have advocated reconstruction of the inferior cul-de-sac, the degree of repair and the necessity for repair being in inverse proportion to the anteroposterior diameter of the lower lid As the diameter, i e., the distance from the tarsal margin of the lid to the lid-socket junction, is increased, there is less indication for surgical intervention As the diameter decreases, up to the point where the lid and the socket are in direct continuity, the indication for operation is increased With this procedure a new sulcus will be formed, which will permit the eye to rest within the socket rather than on the lid, and this will be a great factor in prevention of atony

Exercises of the lower lid in cases of mild atony will frequently restore the tone of the orbicularis muscle Employment of such exercises should be much more stressed than it is after the fitting of a satisfactory prosthesis The patient should be placed in front of a mirror and shown how the lower lid can be raised, utilizing the musculature in the immediate vicinity, especially the orbicularis We suggest that the patient place the finger in region of the eyebrow and produce pressure, so as not to use the frontalis and the orbicularis muscle of the upper lid in closing the eye The principle is to raise the lower lid

In cases of more severe atony, with dropping which borders on ectropion, seen frequently in older patients, operation should be performed even before the artificial eye is inserted The degree of correction necessary can be determined with the first fitting of the wax plug, and the eye need not be completed until the operation has been performed In



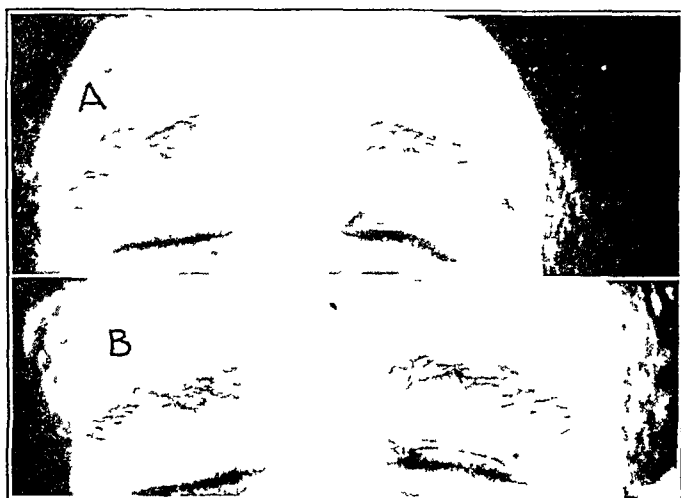


Fig 6—*A*, absorption of soft parts of the left orbital socket, with sunken appearance *B*, repair with insertion of a dermal graft

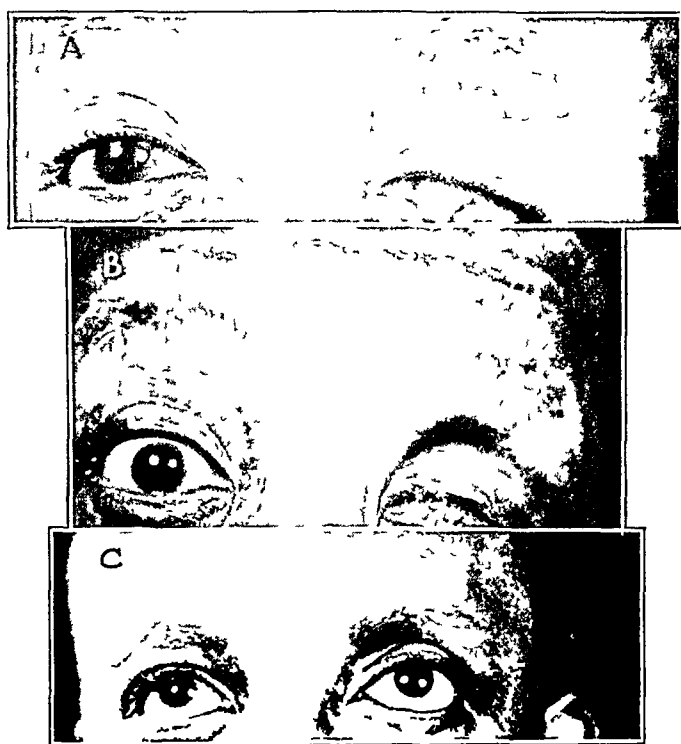


Fig 7—*A*, cicatricial deformity with symblepharon Previous operations had been performed, but the patient still could not wear an artificial eye Scar tissue extended deep into the inferior cul-de-sac This tissue was excised, and a mucous membrane graft was inserted *B*, result of excision of scar tissue and insertion of a mucous membrane graft *C*, patient with the artificial eye in place

the majority of cases of this type we prefer the Kuhnt-Szymanowski<sup>3</sup> procedure for the correction. The Wheeler tarsorrhaphy at the external canthus is ideal for cases of milder atony, but care should be taken with regard to the degree of closure of the palpebral fissure, so that it will not interfere with fitting of the prosthesis. There is no reason in narrowing the palpebral fissure to eliminate a prominent lateral exposure of the sclera when the narrow palpebral fissure will be the most noticeable. Again, we cannot help but stress the importance of giving the patients with mild atony at least three months' trial with exercises prior to any operative procedure. One of the complications encountered with the dropping of the lid is complete relaxation of the external canthal ligament. Repair of the canthal ligament is in order primarily because otherwise if the lower lid is shortened and the edge of the tarsal border reattached retraction of the upper lid will be produced and the upper lid will assume a semicircular appearance rather than its normal outline. Galvanocautery is not indicated in cases of this type. Complete shortening of the lower lid is the procedure of choice.

Other complications are minor defects above the orbit. Such defects are frequently important and are difficult to remedy. In the past too little stress was placed on their repair. It is not sufficient to repair the socket and neglect a notched or distorted lid or a deformity of the eyebrow. A patient will not have a good appearance, with a well fitted prosthesis and a sunken upper socket. In the present mass repair, ophthalmic surgeons are learning a good deal toward the perfecting of reparative surgery about the orbit.

A few of these minor defects are illustrated in this paper. A supplement, showing more pronounced deformities of the lids and orbit and their repair, will be presented at a later date.

#### CONCLUSION

In any circumstances, we feel that prior to operation the prosthetics laboratory should see the patient. With the advent of plastic eyes this is important, since the necessity for operation can be determined in a short time. There must be a closer cooperation of the prosthetics laboratory, the ophthalmologist and the plastic surgeon. True, one will not encounter cases of the type one now comes in contact with. The severity of the condition will not be as pronounced. The underlying pathologic condition will not be as great. But, as has already been mentioned, people are becoming more eye conscious, and it will tax the skill of ophthalmologists to the limit to see that they are properly fitted.

<sup>3</sup> Kuhnt, H, cited by Davis, J. S. *Plastic Surgery Its Principles and Practice*, Philadelphia, P. Blakiston's Son & Co., 1919. Szymanowski, J, cited by Beard, C. H. *Ophthalmic Surgery*, ed 2, Philadelphia, P. Blakiston's Son & Co., 1914.

## INFLUENCE OF LOCAL ANTISEPTICS ON REGENERATION OF CORNEAL EPITHELIUM OF RABBITS

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**D**URING World War II the incidence of ocular injuries was unusually high. Recent reports have pointed out that a wide variety of agents affect adversely the healing of the epithelial defects of the cornea. No agent has yet been discovered which increases the rate of healing.

I<sup>1</sup> have demonstrated that sulfonamide compounds in the form of powder, ointment or emulsion retard the regeneration of the epithelium of the cornea and promote the formation of scar tissue and vascularization. Smelser and Ozanics<sup>2</sup> showed that sulfathiazole and sulfacetimide inhibit cell migration after corneal burns. Sulfadiazine and penicillin produce only slight inhibitory effects. Berens, de Gara and Loutfallah<sup>3</sup> demonstrated that corneal wounds healed more slowly when treated with a sulfonamide ointment or with the ointment base alone than when the wounds were untreated. Sulfonamide ointment delayed the healing of deeper wounds more than that of superficial ones. Leopold and Steele<sup>4</sup> found that the retarding effect of sulfonamide drugs was greater in corneas in which the denudation involved the limbus than in those in which the limbus was not involved. They stated that the differences in retarding or scarring effects between ointment bases or powder bases alone and those containing sulfonamide compounds were insignificant.

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Dr. K. K. Chen and his associates, of the Lilly Research Laboratories, gave valuable aid in this work.

1 Bellows, J. G., and Gluckman, R. Local Toxic Effects of Sulfanilamide and Some of Its Derivatives, *Arch. Ophth.* **30** 65 (July) 1943.

2 Smelser, G. K., and Ozanics, V. Effect of Chemotherapeutic Agents on Cell Division and Healing of Corneal Burns and Abrasions in Rat, *Am. J. Ophth.* **27** 1063, 1944.

3 Berens, C., De Gara, P. F., and Loutfallah, M. Effect of Sulfonamide Ointment on Healing of Experimental Wounds of Rabbit Cornea, *Arch. Ophth.* **30** 631 (Nov.) 1943.

4 Leopold, I. H., and Steele, W. H. Influence of Local Application of Sulfonamide Compounds and Their Vehicles on Regeneration of Corneal Epithelium, *Arch. Ophth.* **33** 463 (June) 1945.

Gundersen and Liebman<sup>5</sup> determined experimentally the effect of local anesthetics on the regeneration of corneal epithelium. The sulfate of butacaine and the hydrochlorides of cocaine, tetracaine, phenacaine and larocaine were found to delay the healing process of the corneal epithelium of the guinea pig. It was demonstrated that the concentration and toxicity of the preparation modify the effects. Smelser<sup>6</sup> reported that the common local anesthetics retard the migration of epithelial cells over the burned area.

Friedenwald and his co-workers<sup>7</sup> studied the mitotic and wound-healing activities of the corneal epithelium. They found that histamine, acetylcholine, physostigmine, carbaminoylcholine chloride and atropine are without effect on the mitotic activity. Epinephrine and ephedrine suppress mitosis. After the removal of the superior cervical sympathetic ganglion, colchicine causes a sharp drop in the rate at which cells enter mitosis. Mechanical damage, ultraviolet and beta radiation, cold, vitamin A deficiency and local and general anesthetics, such as cocaine, ether and barbiturates, inhibit mitosis.

In view of the fact that most surgeons in treating a corneal wound employ an antiseptic to decrease the possibility of infection, and since up to the present time there has been no report showing the effects of antibacterial agents commonly used in ocular therapeutics on the regeneration of the corneal epithelium, the following report is presented.

#### METHOD

Young adult rabbits, weighing approximately 2 Kg, were employed in this investigation. The cornea was anesthetized with a 4 per cent solution of cocaine hydrochloride, chosen not only for its anesthetic qualities but for its drying effect, which facilitated the removal of the epithelium, this was accomplished by rubbing the cornea with dry gauze, to make certain that the entire cornea was denuded of its epithelium, the eyes were stained with fluorescein. The

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5 Gundersen, T, and Liebman, S. D. Effect of Local Anesthetics on Regeneration of Corneal Epithelium, *Arch Ophth* **31**:29 (Jan) 1944

6 Smelser, G. K. Effect of Local Anesthetics on Healing of Burns of the Cornea, *Arch Ophth* **33** 254 (March) 1945

7 Buschke, W., Friedenwald, J. S., and Fleischmann, W. Studies on the Mitotic Activity of the Corneal Epithelium. Methods, the Effects of Colchicine, Ether, Cocaine, and Ephedrin, *Bull Johns Hopkins Hosp* **73** 143, 1943. Friedenwald, J. S., and Buschke, W. The Influence of Some Experimental Variables on the Epithelial Movements in the Healing of Corneal Wounds, *J Cell & Comp Physiol* **23** 95, 1944, The Effects of Excitement, of Epinephrine and of Sympathectomy on the Mitotic Activity of the Corneal Epithelium in Rats, *Am J Physiol* **141** 689, 1944, Mitotic and Wound-Healing Activities of the Corneal Epithelium, *Arch Ophth* **32** 410 (Nov) 1944

course of regeneration was observed by daily examination, facilitated by fluorescein staining

The agents employed in this investigation were instilled in the left eyes of rabbits three times daily, while the right, or control, eye received a similar amount of isotonic solution of sodium chloride. Five rabbits was the minimum number used for each drug. Aqueous solutions of the following substances were investi-

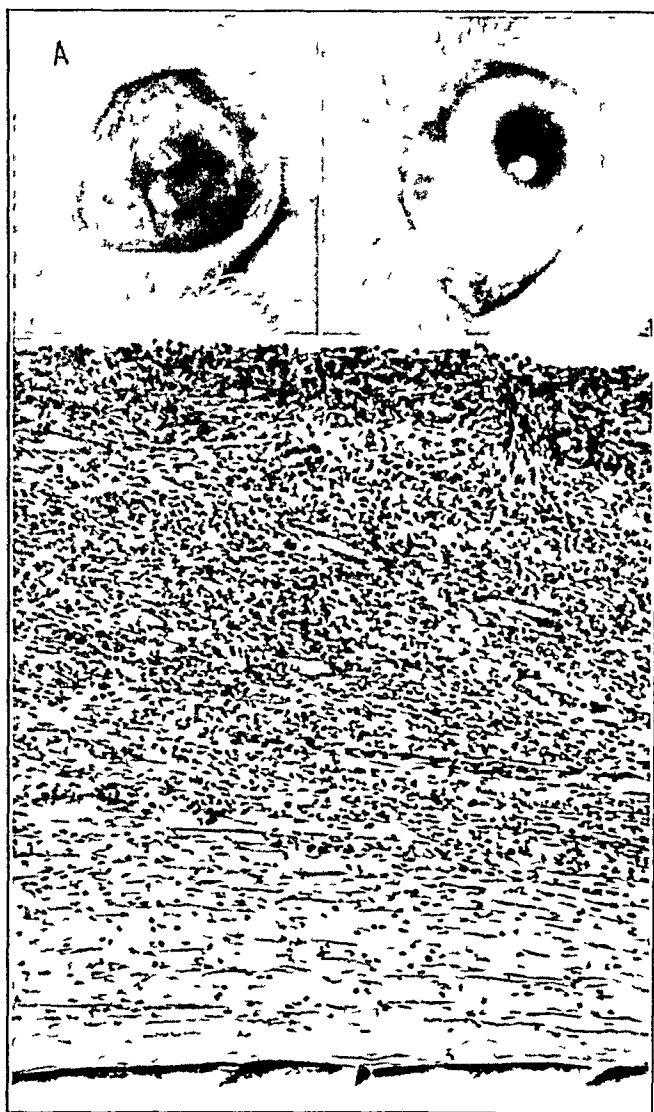


Fig 1—*A*, effect of 10 per cent mild silver protein on the denuded cornea (left) of treated eye and (right) of control eye. *B*, section of cornea treated with mild silver protein ( $\times 111$ )

gated: mild silver protein (10 per cent), zinc sulfate (0.5 per cent), merbromin (2 per cent), phemerol chloride (1:2,500 concentration in 2 per cent boric acid solution), mercuric oxycyanide (1:5,000), metaphen (1:2,500), merthiolate (1:2,500), acriflavine (1:1,000), zephiran chloride (1:3,000), penicillin (1 cc containing 2,500 Oxford units) and sodium sulfathiazole (2 per cent)

# RESULTS

During the first twenty-four hours the treated and untreated eyes were clinically indistinguishable. There was haziness of the cornea and generalized congestion of the conjunctiva. After this period the return of the corneal luster in the periphery of the cornea and the failure of

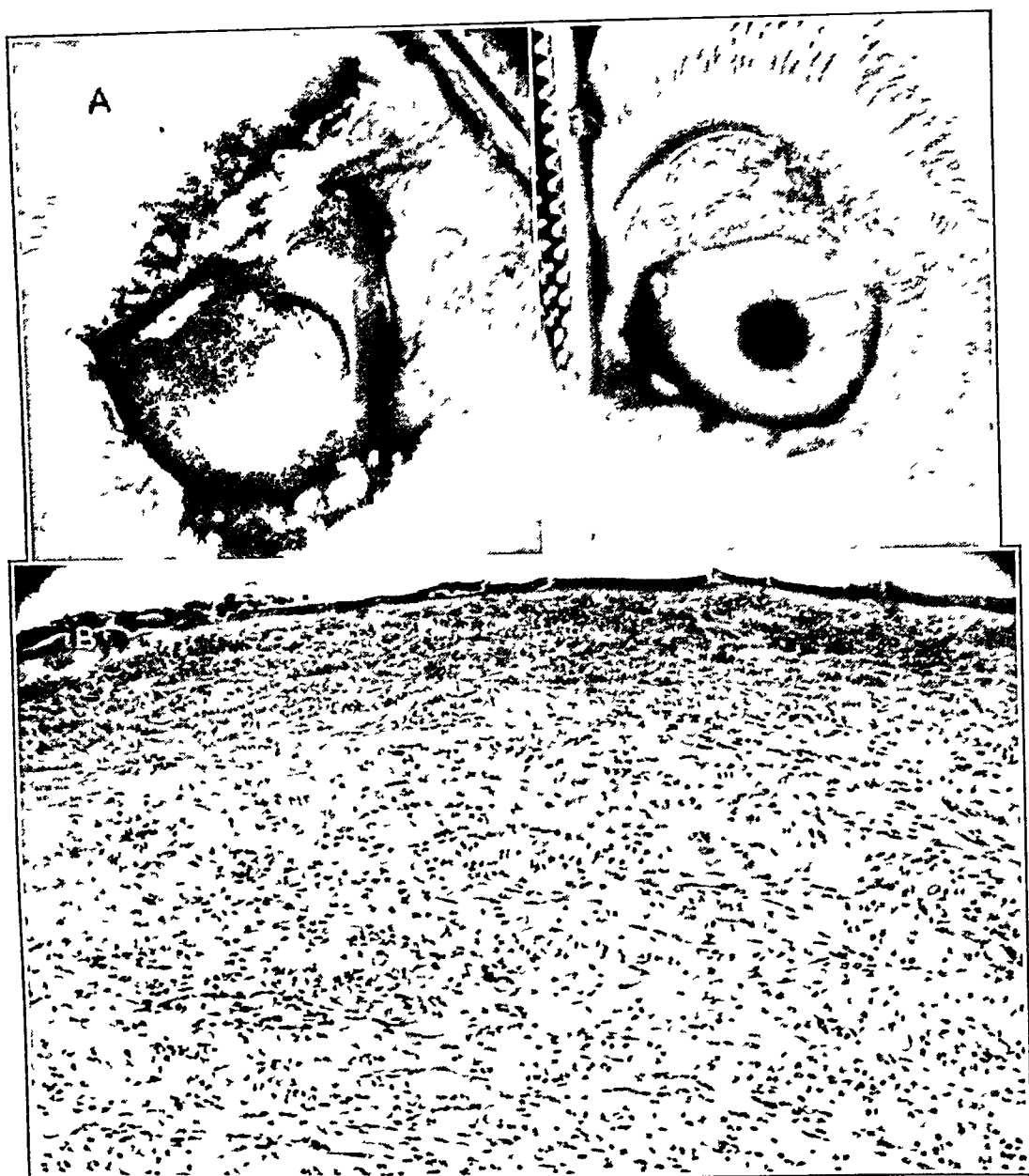


Fig 2—*A*, effect of 2 per cent merbromin on the denuded cornea (left) of treated eye and (right) of control eye. *B*, section of cornea treated with merbromin ( $\times 111$ )

the corresponding area to stain with fluorescein indicated the return of the epithelial covering in that region. Nearly all the untreated eyes appeared clinically normal in four to six days, while the eyes treated with the common local antiseptics still showed large denuded areas (table)

*Mild Silver Protein, 10 Per Cent*—The corneas treated with mild silver protein, even fifteen days after the denudation, had central dark-staining areas, which remained permanently opaque. Vascularization was pronounced (fig 1 *A*). Histologic examination of the corneas removed after fifteen days showed that those of the control eyes were

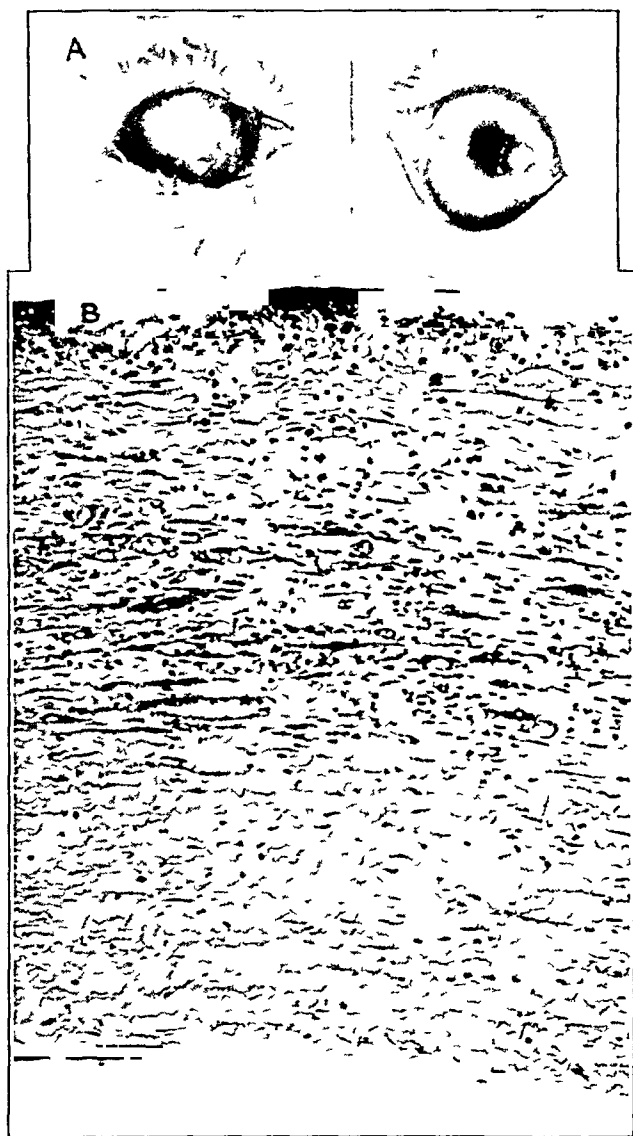


Fig 3—*A*, effect of 0.5 per cent zinc sulfate on the denuded cornea (left) of treated eye and (right) of control eye. *B*, section of cornea treated with zinc sulfate ( $\times 111$ ).

normal. The corneas treated with mild silver protein were thickened by marked leukocytic infiltration and moderate edema. Vascularization was prominent. The epithelium was entirely absent, and the base of the

ulceration consisted of a dense layer of leukocytes, a few fibroblasts and remnants of corneal tissue (fig 1 B)

*Merbromin, 2 Per Cent Solution*—A 2 per cent solution of merbromin greatly retarded the regeneration of the corneal epithelium and finally produced a dense, deep red opacity involving the entire cornea (fig 2 A) Microscopic examination revealed a cornea thickened by edema, leukocytic infiltration and vascularization (fig 2 B)

*Zinc Sulfate, 0.5 Per Cent Solution*—Zinc sulfate in 0.5 per cent solution applied three times daily to the denuded corneas delayed the regeneration of the epithelium. A dense white opacity involving the

*Time Required for Regeneration of Corneal Epithelium*

| Drug                    | Concentration  | Number of Days |             | Condition of Cornea |
|-------------------------|--|----------------|-------------|---------------------|
|                         |  | Treated Eye    | Control Eye |                     |
| Mild protein silver     | 10%  | 15+            | 6           | Opacity present     |
| Merbromin               | 2%   | 15+            | 4           | Opacity present     |
| Zinc sulfate            | 0.5%   | 13             | 4           | Opacity present     |
| Zephiran chloride       | 1:3,000  | 15+            | 4           | Opacity present     |
| Acriflavine             | 1:1,000  | 15+            | 5           | Opacity present     |
| Metaphen                | 1:2,500  | 13             | 5           | Opacity present     |
| Merthiolate             | 1:2,500  | 13             | 6           | Opacity present     |
| Mercuric oxycyanide     | 1:5,000  | 11             | 5           | Opacity present     |
| Sulfonamide compounds * | <div> <div>Powder</div> <div>Emulsion</div> <div>Ointment</div> </div> | 13--           | 5           | Opacity present     |
| Phemerol chloride       | 1:5,000  | 7              | 5           | Clear               |
| Penicillin              | 1 cc = 2,500 Oxford units  | 4              | 4           | Clear               |
| Sodium sulfathiazole    | 2%   | 5              | 4           | Clear               |

\* Data from Bellows<sup>1</sup>

entire cornea resulted from the use of this drug (fig 3 A) Microscopic examination disclosed edema, leukocytic infiltration and vascularization of the cornea (fig 3 B)

*Zephiran Chloride, 1:3,000 Aqueous Solution*—Zephiran chloride in 1:3,000 concentration caused a delay in healing similar to that produced by the aforementioned drugs. At the end of fifteen days there was a dense central scar. Vascularization was conspicuous at the periphery (fig 4 A) Microscopic examination of the cornea removed on the fifteenth day revealed pronounced edema with moderate vascularization and leukocytic infiltration (fig 4 B)

*Acriflavine, 1:1,000 Aqueous Solution*—Acriflavine in 1:1,000 concentration delayed epithelization and caused a dense scar to form in the cornea (fig 5 A) The cornea removed on the fifteenth day revealed



microscopically variations in thickness of the epithelium. Beneath the epithelium were fibroblastic proliferation and cystic spaces, while deeper in the cornea there were edema, vascularization and leukocytic infiltrations (fig 5 B)

*Metaphen, 1 2,500 Aqueous Solution*—Metaphen in 1 2,500 concentration retarded epithelization and produced scar formation of the

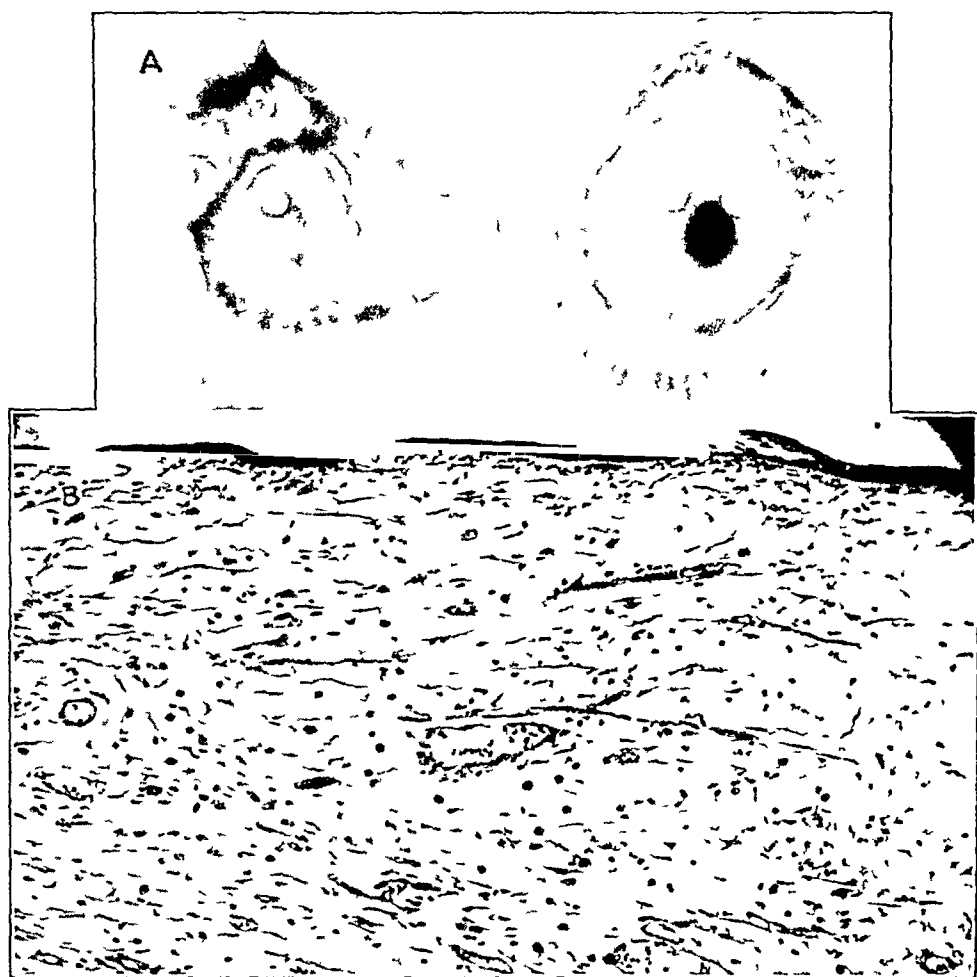


Fig 4—A, effect of zephiran chloride in 1 3,000 aqueous solution on denuded cornea (left) of treated eye and (right) of control eye B, section of cornea treated with zephiran chloride ( $\times 111$ )

cornea (fig 6 A) Histologic examination of the cornea removed on the fifteenth day revealed an edematous, infiltrated and vascularized cornea with fibroblastic proliferation (fig 6 B)

*Merthiolate, 1 2,500 Aqueous Solution*—Merthiolate in 1 2,500 concentration also delayed the epithelization of the cornea, producing scarring with vascularization (fig 7 A) Microscopic examination of

an eye removed on the fifteenth day showed intense corneal edema with a moderate degree of vascularization and leukocytic infiltration (fig 7 B)

*Mercuric Oxycyanide, 1 5,000 Aqueous Solution*—Mercuric oxycyanide in 1 5,000 aqueous solution caused a delay in epithelization of the denuded cornea and produced a permanent scar on the cornea (fig 8 A) Histologic examination revealed that the cornea was thick-

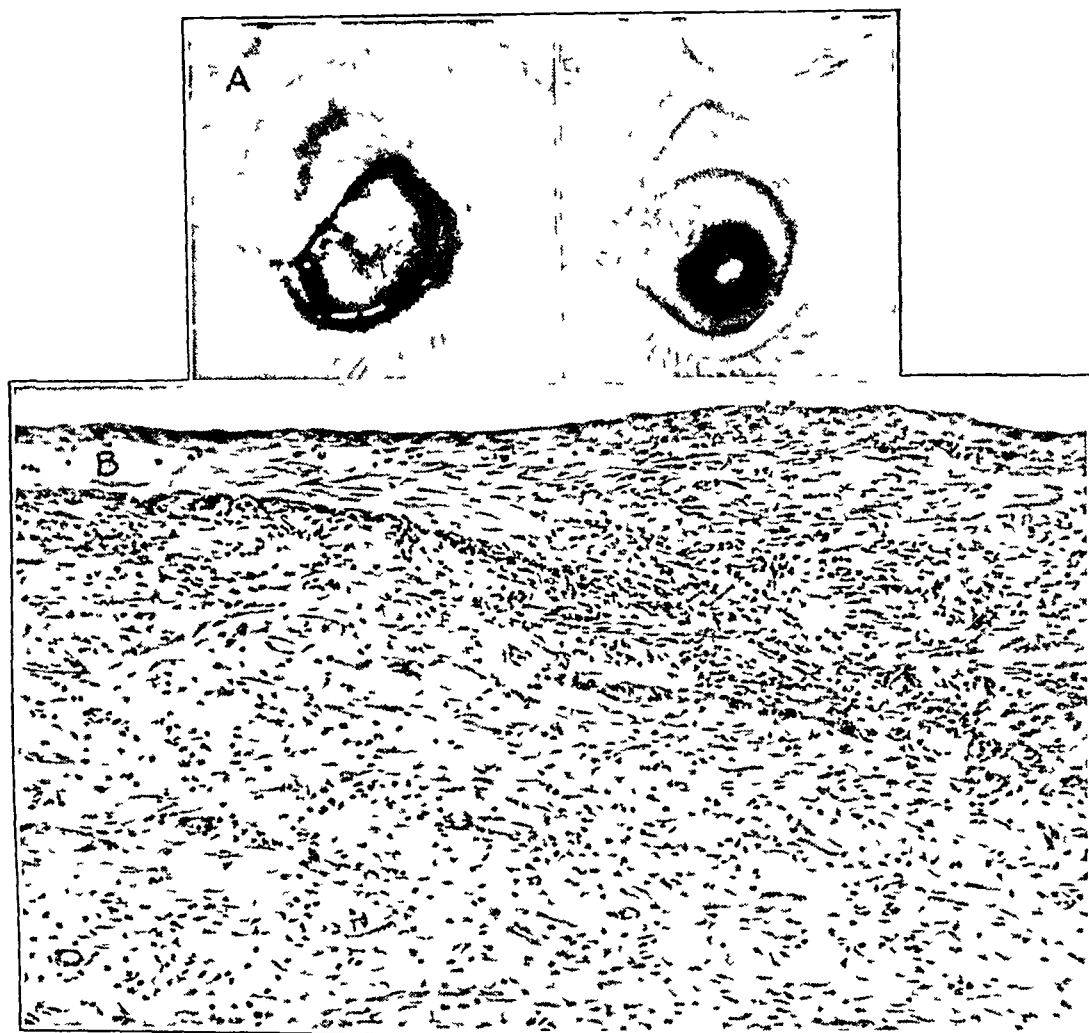


Fig 5—A, effect of acriflavine in 1 1,000 solution on the denuded cornea (left) of treated eye and (right) of control eye B, section of the cornea treated with acriflavine ( $\times 111$ )

ened by edema, leukocytic infiltration and vascularization Fibroblastic proliferation was found beneath the epithelium (fig 8 B)

*Sulfonamide Compounds*—In a previous report<sup>1</sup> it was shown that sulfanilamide, sulfathiazole, sulfadiazine and sulfapyridine applied to the denuded cornea in the form of a powder, ointment or emulsion delayed the reformation of the epithelial layer and caused a scar to form on the

cornea In the present investigation, a 2 per cent solution of sodium sulfathiazole caused neither delay in epithelization nor scarring of the cornea

*Phemerol Chloride, 1 5000 Aqueous Solution*—Phemerol chloride in 1 5,000 concentration in 2 per cent boric acid solution delayed

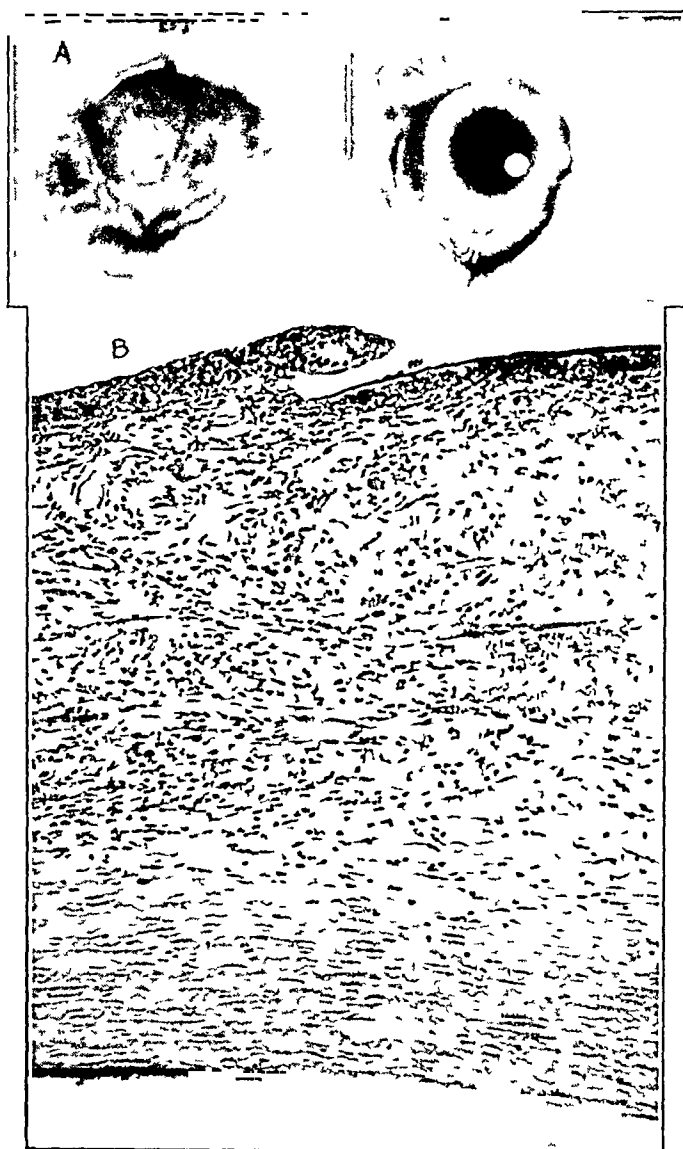


Fig 6—*A*, effect of a 1 2,500 aqueous solution of metaphen on the denuded cornea (left) of treated eye and (right) of control eye *B*, section of cornea treated with metaphen ( $\times 111$ )

epithelization by only a few days No permanent opacity formed on the cornea, and histologic examination disclosed an unaltered cornea (fig 9)

*Penicillin* (1 cc containing 2,500 Oxford units) —Penicillin neither delayed the regrowth of the epithelium of the cornea nor caused scar formation. Microscopic examination disclosed no changes in the cornea (fig 10)

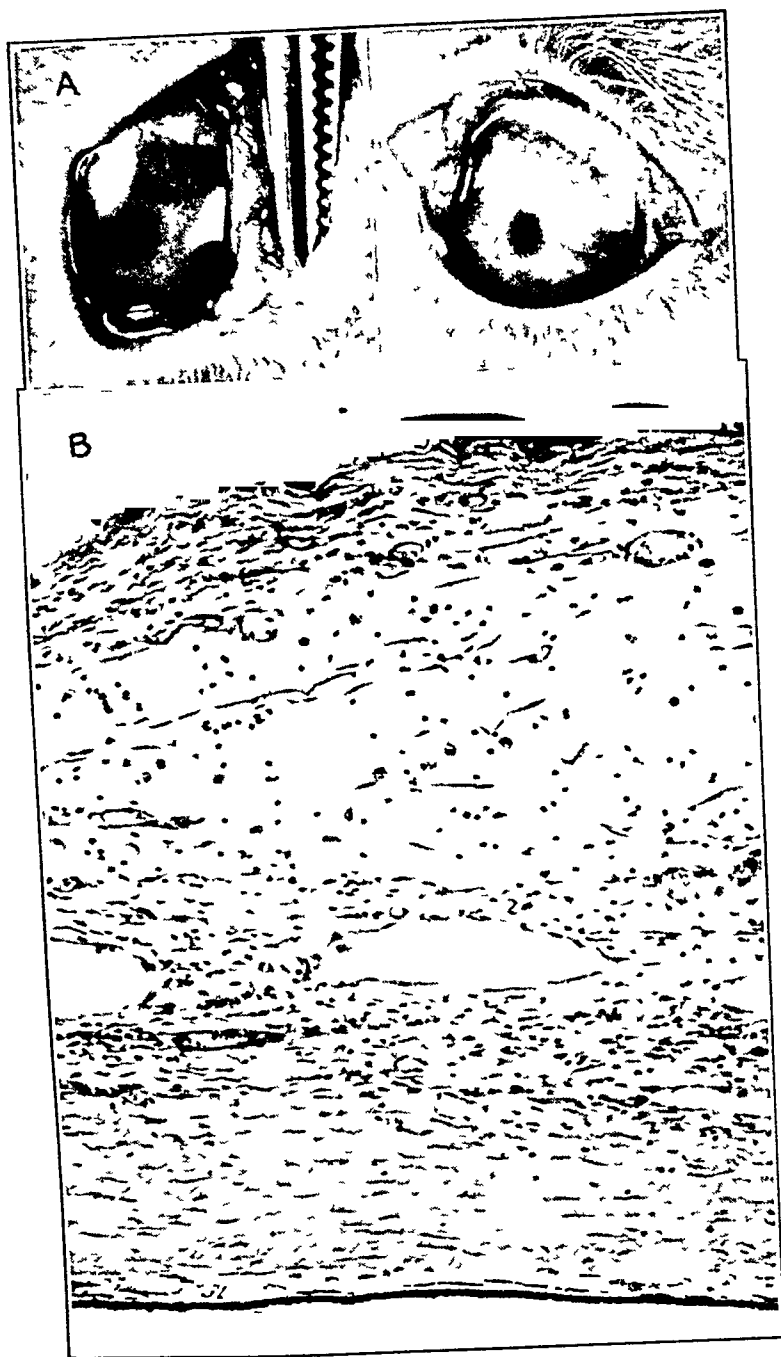


Fig 7—*A*, effect of a 1:2,500 per cent aqueous solution of merthiolate on the denuded cornea (left) of treated eye and (right) of control eye. *B*, section of cornea treated with merthiolate ( $\times 111$ )

#### SUMMARY AND CONCLUSIONS

The results of this investigation disclosed that the local antiseptics ordinarily employed in ocular therapeutics (mild silver protein, merbromin, zinc sulfate, zephiran chloride, acriflavine, metaphen, merthio-

late and mercuric oxycyanide) had considerable delaying effect on the healing process of the corneal epithelium of rabbits. In most instances these drugs caused a permanent opacity of the cornea. Microscopic examination of the corneas showed edema, leukocytic infiltration, fibroblastic proliferation and vascularization. Since the same histologic

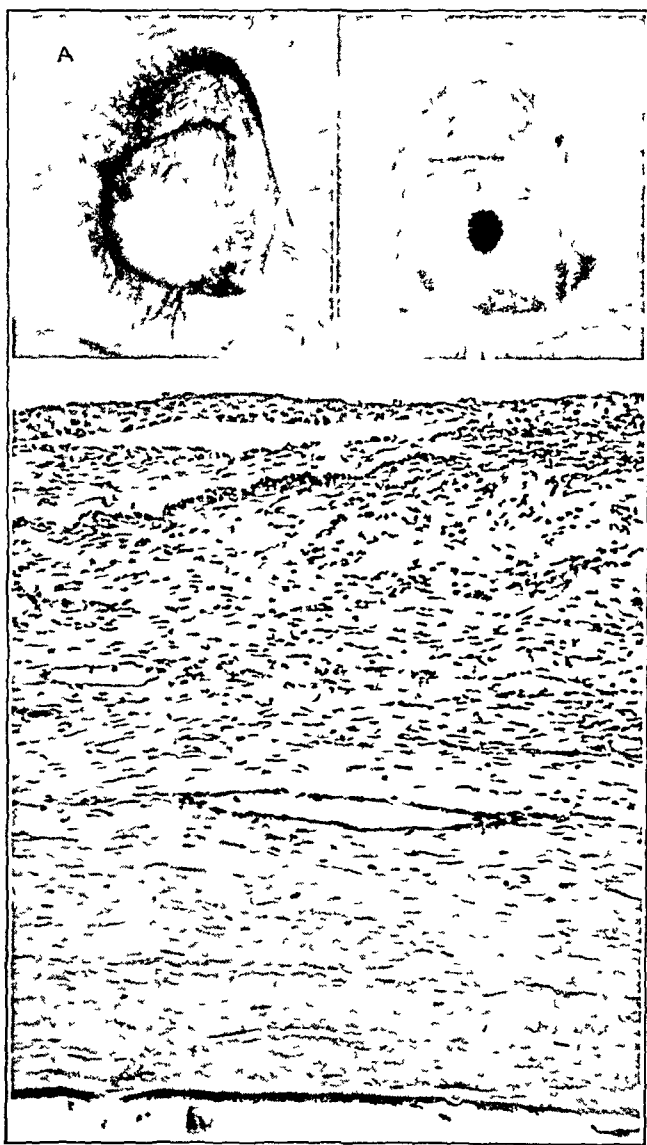


Fig 8—*A* effect of mercuric oxycyanide in 1:5,000 aqueous solution on the denuded cornea (left) of treated eye and (right) of control eye. *B*, section of cornea treated with mercuric oxycyanide ( $\times 111$ )

changes were produced by various therapeutic agents differing greatly in chemical constitution, it would appear that the corneal changes were due to a nonspecific irritation rather than to a specific chemical effect.

Phemerol chloride in 1 5,000 concentration in 2 per cent boric acid solution delayed the healing only slightly and produced no permanent alterations in the cornea. Sodium sulfathiazole, in 2 per cent aqueous solution, and penicillin, in a concentration in which 1 cc contained 2,500 Oxford units, neither delayed the regeneration of the epithelial covering nor produced corneal opacities.

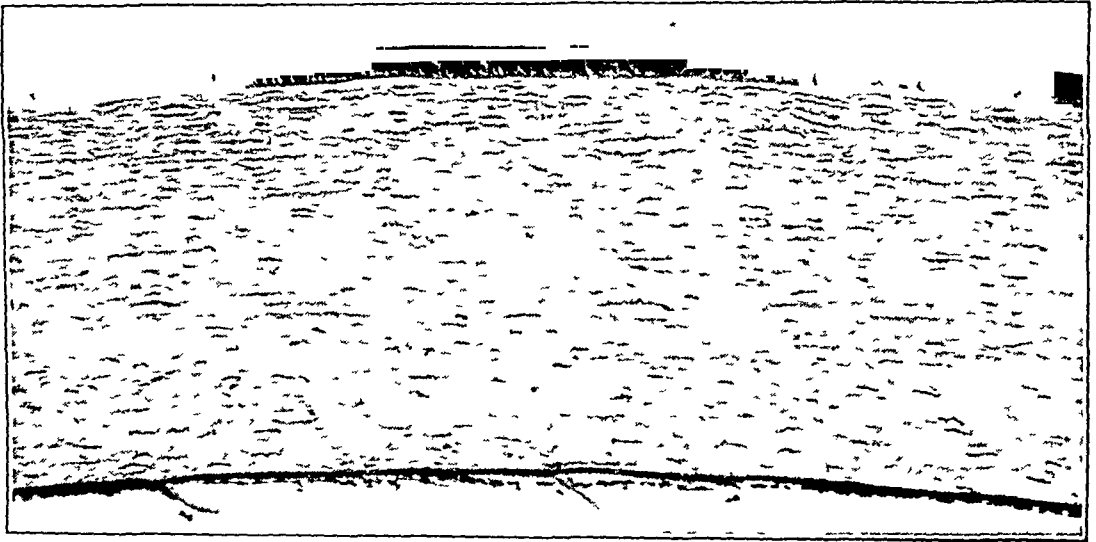


Fig 9—Section of cornea treated with phemerol chloride 1 5,000 concentration in 2 per cent boric acid solution ( $\times 111$ )

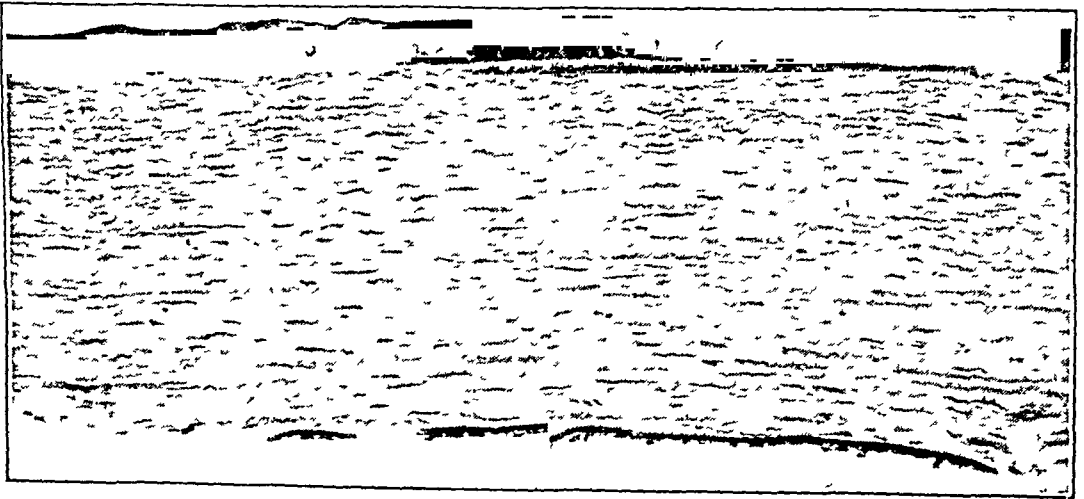


Fig 10—Section of cornea treated with penicillin (1 cc containing 2,500 Oxford units) ( $\times 111$ )

In conclusion, repeated instillations of the common local antiseptics are not recommended in the treatment of corneal injuries. When the possibility of infection is great, the aqueous solution of sodium sulfathiazole or penicillin may be used.

## HEREDITARY DISK-SHAPED (RING) CATARACT

Report on a Family, with Microscopic Examination of an Eye

ENRIQUE SAMUEL HARO, M D

LIMA, PERU

THE DISK-SHAPED, or ring, cataract is a rare form of congenital cataract that has been reported relatively few times. Judging from a review of the literature, the hereditary tendency has been reported in only 1 family. In July 1944 a 10 year old girl (Nadine L.) with congenital disk-shaped cataracts was brought to the eye clinic of Stanford University Hospital for examination and treatment. Her history led to the study of a most interesting family, consisting of 59 persons, of whom 16 have the same congenital anomaly.

In addition to the cataract, all the affected members examined showed symmetric dislocation of the lens. No other local or systemic anomalies were found. This family is not related to any other with congenital cataract, and, so far as I can trace the familial history, there were no known cases of this condition prior to the ones reported herein. There was no history of consanguinity.

One of the eyes examined was enucleated after a traumatic laceration and was studied microscopically.

The study of congenital hereditary cataract has shown that there is a tendency to uniformity in the type within any family line. However, while this is usually true, Lutman and Neel<sup>1</sup> pointed out that it is sometimes found that certain of the cataractous persons in a given pedigree have a type of opacity of the lens that differs materially from the type present in other affected members of the family. Of interest in any hereditary condition is the exact nature of the defect, its origin, when suddenly appearing in a healthy strain of persons, the mode of transmission, and the variability within the group. However, congenital cataract must not be regarded merely as an opaque lens, it is "a part of the whole cycle of events". Often other abnormalities are present. All this involves an important sociologic problem, especially

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Dr Haro made this study while holding the Kellogg Foundation Scholarship in the Department of Ophthalmology, Stanford University School of Medicine, San Francisco.

1 Lutman, F. C., and Neel, J. V. Inherited Cataract in the B Genealogy, Arch Ophth **33** 341 (May) 1945.

2 Fox, L. W. Congenital Cataract, J A M A **89** 2249 (Dec 31) 1927.

if it is true, as Nettleship<sup>3</sup> and others have stated, that persons with hereditary imperfections and disease are as a rule members of unusually large pedigrees

#### CLINICAL APPEARANCE OF DISK-SHAPED CATARACT

The disk-shaped cataract is characterized by the presence of a central opacity at a distinctly deeper level than the remainder of the surface of the lens, with some irregular opacities in the immediate vicinity of the central patch, in which the latter appears to be engraved. With a small pupil the central opacity may fill the entire pupillary area, if sufficient dilation is obtained, a peripheral clear zone can be seen.

The lens in some instances appears smaller than usual. It is thin anteroposteriorly, especially in the center, owing to the absence of the central structures. This hollowed portion is closed by a membrane.

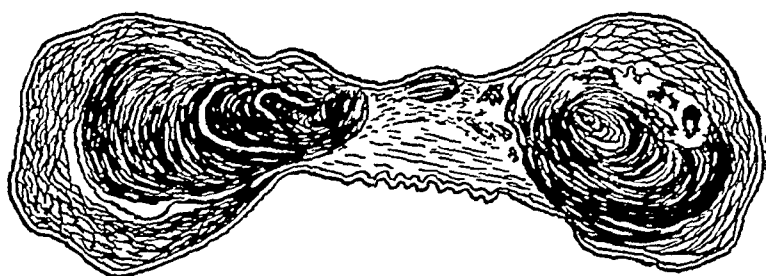


Fig 1—Sagittal section of a disk-shaped, or "ring" cataract. The lens appears as a dumbbell, having two lateral masses connected by a central band.

more or less thick and opaque, similar to a secondary cataract. This laminated mass of tissue, according to pathologic studies (fig 5), consists of three layers: the anterior and the posterior lens capsule, with the remains of the epithelium of the lens, showing a variable amount of proliferation, between them. There is no intermediate lens substance proper in this portion. In all the rest of the lens cortex is present, but with some disturbance around the central defect. This defect forms an opaque ring, becoming clearer toward the periphery. The opacity within the ring itself has in most cases a similarity to lamellar cataract, with several concentric zones.

The central defect varies in size and corresponds roughly to the diameter of the embryonic nucleus.

The lens as a whole has the shape of a ring, like a life belt. In sections it appears as a dumbbell, having two lateral masses connected by a central band (fig 1).

<sup>3</sup> Nettleship, E. On Some Hereditary Diseases of the Eye, *Tr Ophth Soc U Kingdom* 29:57, 1909.



## PEDIGREE OF THE L FAMILY

Compiling the family data of the reported cases was rather difficult, inasmuch as many members live in other states. The few in San Jose, Calif., willingly gave information as accurately as possible. They did not know personally several members of the family, moreover, the oldest one alive was the ninth child of his sibship, and some of his brothers and sisters died before he was born or when he was too young to remember any relevant facts about them. However, the information obtained after several rechecks with various relatives, with elimination of the doubtful facts, can be considered dependable. The family contacts have been fairly close. All the informants were deeply concerned about the condition present in such a high percentage in the family and remembered rather accurately the facts related to it.

About the middle of the last century the first members of the family of whom anything is known came to the United States and settled in Springfield, Mo. A detailed description of the genealogy follows.

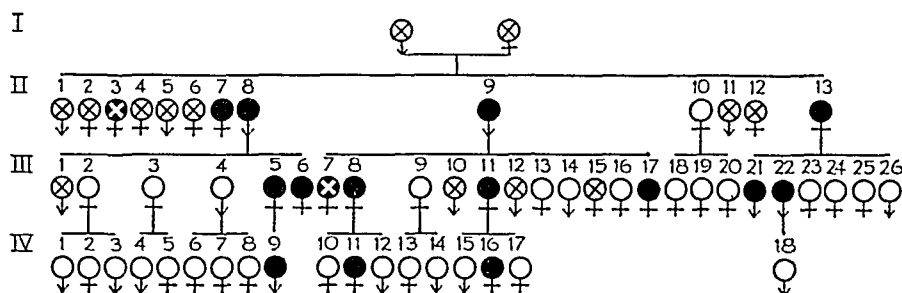


Fig 2—Family tree. Affected members are indicated by black circles, members who have died, by circles with crosses, and affected members who have died, by black circles with white crosses.

I 1<sup>4</sup> Mr France L came from Ireland. He was a healthy man and had good vision. Late in his life he wore glasses "just for reading." He died at the age of 74 of some type of renal disease.

I 2 Mrs Sara L came from England. She was known to have good vision and to be healthy. She also wore glasses for reading only late in her life. She died of a "stroke" at the age of 72.

This marriage had an issue of 13 children.

II 1 Virgil L was not affected. He died at the age of 3 months of diphtheria.

II 2 Clara L was not affected. She died at the age of 7 months of pneumonia.

II 3 Beckey L had congenital cataracts. She died at the age of 19 of typhoid.

II 4 Carmen L was not affected. She died at the age of 22 as a result of an accident.

4 The Roman numeral indicates the generation, the arabic numeral, the individual number in the family generation (fig 2).

- II 5 Oscar L was not affected He died at the age of 17 as a result of an accident
- II 6 X L. was a stillborn girl
- II 7 Myrthle L was 62 years old, she had congenital cataracts She had been seen by ophthalmologists but had never had an operation Her vision was very poor, she could see only large objects and was unable to read She was a widow and had no children
- II 8 William L was 60 years old He had congenital cataracts but had had no operation He could see just "enough to get around" but could not read He was married and had 6 children
- III 1 Otis L was not affected He died at the age of 10 years of whooping cough
- III 2 Opal P, aged 34, was not affected She was married and had 3 children
  - IV 1 Pat P, aged 13, was not affected
  - IV 2 Dorothy P, aged 10, was not affected
  - IV 3 James P, aged 8, was not affected
- III 3 Leora S, aged 31, was not affected She was married and had 2 children
  - IV 4 Edward S, aged 14, was not affected
  - IV 5 Joan S, aged 10 was not affected
- III 4 Lye L, aged 29, was not affected He was married and had 3 children.
  - IV 6 Evelyn L, aged 8, was not affected
  - IV 7 Lucell L, aged 6, was not affected
  - IV 8 Loretta L, aged 4, was not affected
- III 5 Helen L, aged 21, had congenital cataracts and was operated on three times ("needlings") Good vision was obtained, which allowed her to go through school successfully She was married and had 1 child
  - IV 9 Joe L, aged 3, had congenital cataracts, vision seemed to be very poor He had had no medical attention at the time of the study
- III 6 Wally L, aged 14, had congenital cataracts Four needling operations were performed, with resulting fairly good vision She was going to school

All the persons so far spoken of, descendants of William L (II 8), live at Springfield, Mo

- II 9 Grover L,<sup>5</sup> aged 56, was the next member of the second generation When he was a few months old, his eyes were examined, and the diagnosis of congenital cataracts was made He was seen by several ophthalmologists, but no operation was attempted, he did not know why He had noticed no decided change in vision, he also stated that he could see better at night General examination showed a tall, apparently strong and healthy man

*Ophthalmologic Examination*—The patient had an esotropia of about 15 degrees, fixing with the left eye most of the time External examination revealed nothing abnormal

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<sup>5</sup> This patient was examined in the present study

Vision with a small pupil was limited to perception of hand movements at 5 feet (15 meters) in the right eye and to counting fingers at 5 feet in the left eye. He could not read at all with the right eye. He read Jaeger type 20, poorly, with the left eye, holding the card very close. The pupils were dilated with eucatropine hydrochloride, 3 per cent, under this condition vision was limited to perception of hand movements at 5 feet and to counting fingers at 10 feet (3 meters) in the left eye. Manifest refraction showed no improvement in the right eye, but vision in the left eye with a +11.00 D sphere, improved to 15/200, with a +3.00 D sphere addition, he read Jaeger type 10 to 12.

Examination with the slit lamp revealed interesting features (fig 3).

**Right Eye** The anterior chamber was deep, there was pronounced iridodonesis, and the lens was dislocated nasally and upward, leaving a rim temporally and inferiorly through which the zonular fibers could be seen. The whole lens was opaque and seemed somewhat smaller than usual, it could be described as

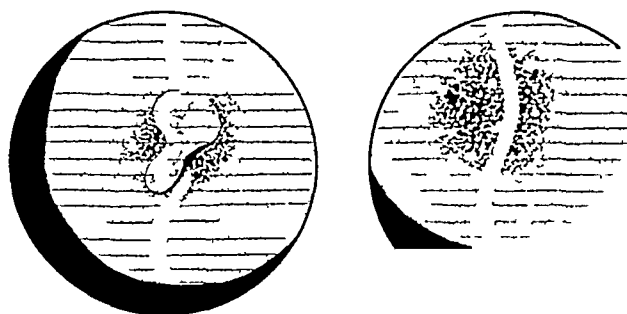


Fig 3—Eyes of Grover L. (II 9) The sketch represents the appearance of the lenses as seen with the slit lamp. Both lenses are white, doughnut-shaped and greatly dislocated, especially the left. The central hollow of the right lens is filled with white, loose material.

a “white doughnut,” with the center partially filled with loose, flocculent material, such as is seen after a dissection, placed behind the capsule and at a deeper level than the periphery of the lens. The central pitlike portion could barely be seen because of the loose material which filled it.

**Left Eye** The chamber was also deep, with pronounced iridodonesis. The lens was small and extremely dislocated nasally and upward, so that the equator formed a broad crescent, with the edge of the dilated pupil in the inferior third, through which the fundus could easily be seen. The whole lens was opaque, and the name “white doughnut” was more appropriate for the lens on this side than for that on the other, as the central portion was very thin, almost clear, with just a fine membrane partially hidden behind the pupillary border superiorly (fig 3). The zonular fibers were present only at the edges of the crescent.

**Fundus** The fundus was not well seen in the right eye, no abnormalities were noted in the left.

**Descendants**—He was married and had 11 children.

III 7 Lucille L. had congenital cataracts and died at the age of 9 of typhoid.

III 8 Maudie D.,<sup>5</sup> aged 30, had congenital cataracts. She was operated on four times when she was 17 years of age. It was stated that such operations were “needlings,” but clear and sharp cuts at either side of the fairly dense membrane in each eye suggested another type of intervention.

Vision was 20/200 in the right eye (with +11.00 D sph  $\ominus$  +1.50 D cyl axis 90) and 20/30 in the left eye (with +11.50 D sph). The patient read Jaeger type 12 with the right eye and Jaeger type 4 with the left eye (with a +3.00 D sphere addition).

External examination revealed nothing abnormal. The pupils were clear, after dilation, rests of fairly dense membranes could be seen, as already stated.

The fundi showed no abnormalities.

She was married and had 3 children.

IV 10 Dolores D,<sup>5</sup> aged 8 was not affected.

IV 11 Doris D,<sup>5</sup> a clinic patient, was 5 years old at the time of the study. The parents noticed cataract in both eyes at the age of 2½ months. Vision seemed not to have changed up to the time of this examination.

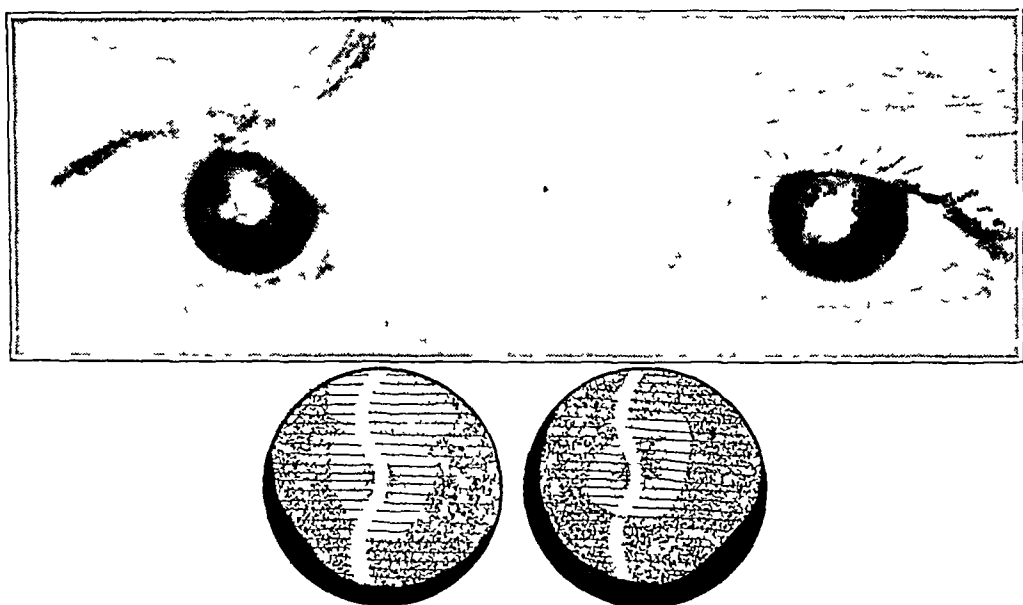


Fig 4—Eyes of Doris D (IV 11). Note the clear periphery and the opaque, hollowed center in each lens. The right eye was enucleated after an injury, so that a pathologic study was possible. See the pathologic report and the photomicrographs (fig 5).

*Ophthalmologic Study*—On the child's entry, vision was limited to perception of hand movements at 1 foot (30 cm) in the right eye and of hand movements at 6 feet (18 meters) in the left eye. (It was not improved after dilation of the pupil.) External examination revealed nothing abnormal except for bilateral "searching" nystagmus. Examination with the slit lamp showed an interesting condition.

**Right Eye** With a dilated pupil, the lens as a whole appeared like a "doughnut," with the three parts characteristic of this type of cataract: the clear periphery, the central opaque membrane, at a deeper level than the periphery, and an intermediate zone, also opaque, with clear cortex anteriorly. The last structure was placed superiorly and extended from the edge of the hollowed center to the equator (fig 4). The lens was dislocated nasally and upward, leaving a well defined rim temporally and inferiorly, through which the zonular fibers could be seen, except for a small portion where the edge of the lens was somewhat flattened.

**Left Eye** With dilated pupil, the appearance of the lens was similar to that of the lens in the right eye. The dislocation was symmetric, there was also a flattened portion. In this lens there were only two parts: the white, opaque and hollowed central area, well outlined, and a clear periphery (fig 4).

The fundi showed no abnormalities.

**Operation**—Three dissections were performed on the left eye, but they were only partially successful, as the tough central opaque portion could hardly be cut. The small openings made were closed almost completely. In the fourth operation, de Wecker's scissors were inserted through a keratome incision and the membrane was cut, obtaining a large pupillary opening. Vision improved to 20/200 (with a correction of +11.00 D sph). Unfortunately, the right eye had to be enucleated after a traumatic laceration near the ciliary body with extensive loss of vitreous. Examination of the specimen confirmed the clinical diagnosis as to the type of cataract, as will be seen from the pathologic report and the photomicrographs (fig 5).

IV 12 Charles D,<sup>5</sup> aged 4 years, was not affected.

III 9 Mildred B, aged 28, was not affected. She was married, and had 2 children.

IV 13 Ettarey B,<sup>5</sup> aged 10, was not affected.

IV 14 Ronald B,<sup>5</sup> aged 3, was not affected. Ophthalmologic examination showed remains of the pupillary membrane (from 7 o'clock to the center of the pupil in the left eye).

III 10 X L, a boy, died a few hours after birth.

III 11 Vera T,<sup>5</sup> aged 25, a clinic patient, had congenital cataracts and was operated on when 15 years old. Four needlings were performed, and fairly good vision resulted.

**Ophthalmologic Study**—**Right Eye** 15/100 (with +12.00 D sph). **Left Eye** 15/70 (with +12.00 D sph). She read Jaeger type 12 with the right eye and Jaeger type 10 (with +3.00 D sph addition) with the left eye. External examination showed exotropia of about 15 degrees. Examination with the slit lamp showed a deep anterior chamber in both eyes. With dilated pupils, a moderately opaque membrane with a clear large opening in both pupillary areas could be seen. The fundi were normal.

**Descendants**—She is married and has 3 children.

IV 15 Billy T,<sup>5</sup> aged 5, was not affected.

IV 16 Mary T,<sup>5</sup> aged 4, a clinic patient, was 2 months old when the presence of cataracts was noted. Vision seemed to be fair, and better in the left eye, although no accurate test was possible. External examination revealed nothing significant except for a pronounced exotropia, the patient fixing with the left eye.

**Ophthalmologic Examination**—Examination with the slit lamp after dilation of the pupils revealed the following condition.

**Right Eye** There was moderate dislocation of the lens, nasally and upward, leaving a narrow rim below. The zonular fibers were intact. The lens itself had three parts: a central opaque, somewhat hollowed area, an intermediate zone, less opaque, with clear cortex anteriorly, extending mostly to the temporal side, above, and a clear periphery (fig 6).

Left Eye There was a symmetric dislocation of the lens, which consisted of two well defined parts the clear periphery and a central white ring with a very deep and clear center This ring was about one-third the total diameter (fig 6)



Fig 5—*A*, anterior part of the eye enucleated from Doris D (IV 11), showing the "annular" cataract *B*, microscopic appearance of the lens at the edge of the central "patch" (see pathologic report)

The fundi were normal This patient had had no surgical treatment as yet

IV 17 Marge T,<sup>5</sup> aged 1 year, was not affected

III 12 Frances L was not affected She died at the age of 11 years of diphtheria

- III 13 Guleen F, aged 20, was not affected She was married and had no children
- III 14 Roy L,<sup>5</sup> aged 17, was not affected
- III 15 X L, a girl, was stillborn
- III 16 Irene L,<sup>5</sup> aged 14, was not affected Examination revealed a strand, remnant of the pupillary membrane, running from 8 o'clock to the center of the lens in the left eye
- III 17 Nadine L,<sup>5</sup> aged 10, was a clinic patient At the age of 2 months cataracts were discovered in both eyes They seemed not to have changed since that time Vision also had not changed On her admission visual acuity was 4/200 in the right eye and 20/200 in the left eye

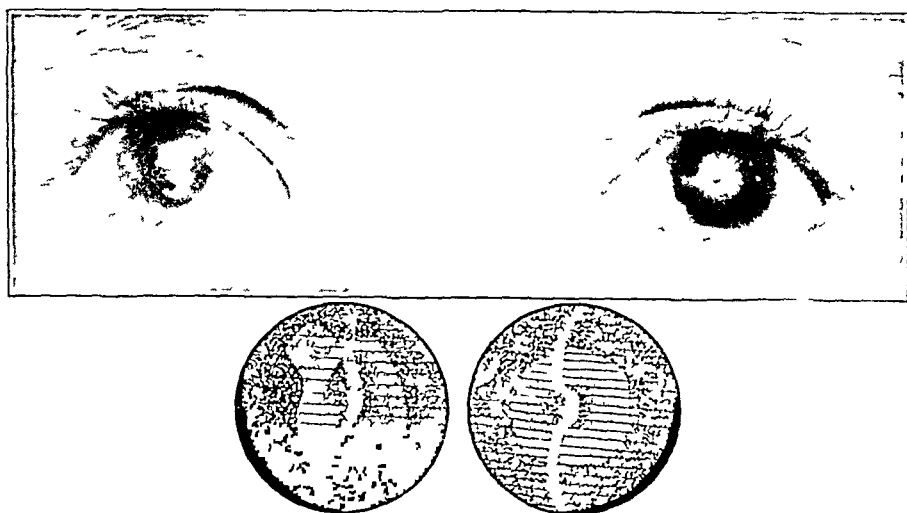


Fig 6—Eyes of Mary T (IV 16) Both lenses are slightly dislocated The right one represents a moderately hollowed, opaque central patch with some surrounding irregular opacities and a clear periphery The left lens has a central ring with a deep clear center The periphery is also clear

This girl had been to school and had learned some letters of the alphabet but was unable to read

External examination revealed nothing of significance

*Examination with Slit Lamp*—Right Eye The lens was dislocated nasally and upward, leaving a rim below, where the zonular fibers were present Three zones could be distinguished a narrow, transparent peripheral one, a large, concentric, opaque portion, with clear cortex anteriorly, and a hollowed central area, partially covered with a white, diamond-shaped membrane, attached above and below to the rest of the opacity and leaving at either side a rim, through which the bottom of the central hollow could be seen (fig 7)

Left Eye The lens appeared smaller than usual and was dislocated upward and nasally to a greater extent than the lens in the right eye, with a rim of intact zonular fibers Three portions could also be seen in this lens a narrow, transparent peripheral zone, a dense, opaque subcortical zone and a large central hollow zone The last, which was situated very deep, was square with sharply cut edges, formed only by a fairly dense membrane, which became clearer toward

the center This portion appeared as though a part of the lens had been excised with a sharp instrument (The inset in figure 7 gives a fair idea of it)

The fundi were normal

*Operation*—Two discissions were performed in the right eye, both of them with Ziegler's needle After the first discission, the large amount of debris practically covered the opening made The second one was more successful, a small opening persisting above the center, however, the central membrane was very tough A third operation was done Wecker's scissors were inserted through a keratome incision and the central membrane was cut, and a large clear opening was obtained

Resulting vision was 20/70 (with a correction of  $+11.00$  D sph  $\subset +1.00$  D cyl, axis 120)

The left eye had not been operated on as yet

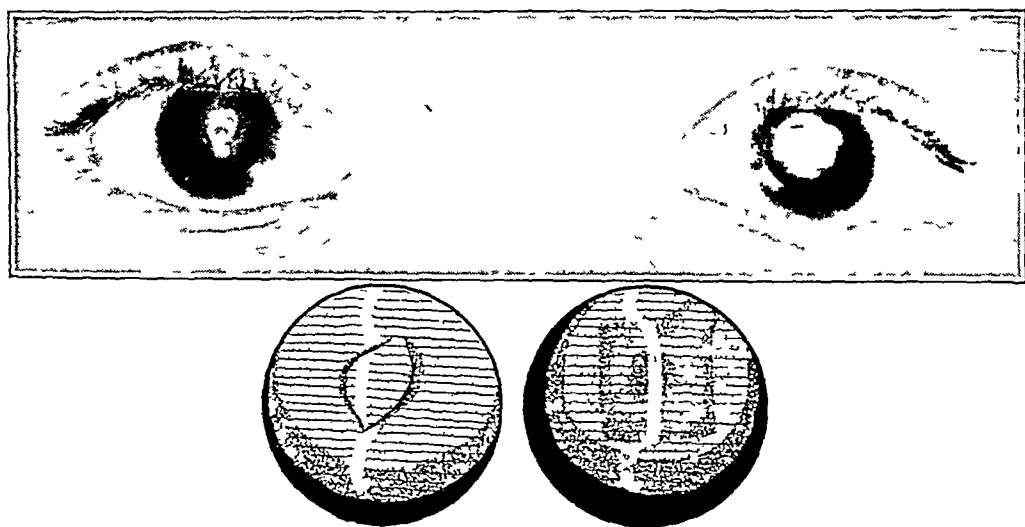


Fig 7—Eyes of Nadine L (III 17) Note the symmetric dislocation of the lenses and their three zones The center is hollowed and diamond shaped in the right eye and square in the left eye Surrounding this are a zone of diffuse opacity and a clear periphery The reflection of the light prevents a clear view of the actual depth of the center

All these persons, descendants of Grover L (II 9) live at San Jose, Calif Only 5 of them are clinic patients, the others have been examined at home

II 10 Sady R, aged 53, the next member of the second generation, was not affected She was married and had 3 children

III 18 Pauline R, aged 32, was not affected She was married and had no children

III 19 Wilma R, aged 30, was not affected

III 20 Betty R, aged 21, was not affected She was married and had no children

II 11 X L, a boy, died a few hours after birth

II 12 X L, a girl, was stillborn

II 13 Jessy D, aged 51, had congenital cataracts She had never had an operation Vision was very poor, she was barely able to do her house-work She could not read She was married and had 6 children



- III 21 Paul D, aged 29, had congenital cataracts He was operated on (two needlings), but the resulting vision was apparently not good He could not read at all, seeing only well enough "to get around" He was married and had no children
- III 22 Victor D, aged 22, had congenital cataracts Four discissions were performed, and fairly good vision was obtained He was able to read and had practically no handicap due to his eyes He was married and had 1 child
- IV 18 X D, a boy, 3 months old, was not affected(?)
- III 23 Mary D, aged 20, was not affected She was married and had no children
- III 24 Ruby D, aged 17, was not affected
- III 25 Jessy D, aged 15, was not affected
- III 26 Virgil D, aged 12, was not affected

These persons, descendents of Mrs Sady R, live at Buffalo, Mo

#### PATHOLOGIC EXAMINATION

The following report was made on the examination of the right eye of Doris D (IV 11), which was enucleated after a traumatic laceration (Laboratory of Ophthalmic Pathology of the University of California)

*Gross Examination*—The specimen consisted of the anterior part of the right eye, previously sectioned through the equator and measuring 23 by 24 by 23 mm

"There was a scar 5 mm behind the limbus in the 9 o'clock position The cornea was clear, showing a widely dilated pupil and a centrally opaque lens The lens was luxated slightly superiorly, permitting a view into the vitreous between the lower margin of the pupil and the equator of the lens Viewed from behind, this luxation was more apparent, showing the lower temporal portion of the equator, separated some distance from the ciliary processes There was, however, no tendency for the lens to 'hinge' The equatorial diameter was about normal

"The lens resembled a doughnut, with a central thinned, membranous area, 2.5 to 3 mm in diameter, which was gray-white The surrounding ring structure possessed the body of lens substance but showed yellowish opacities extending from the membranous portion toward the equator The equatorial portion of the lens showed less cataract formation, appearing almost normal"

*Microscopic Examination*—The circumcorneal tissues, the cornea, the limbus, the anterior chamber and the iris presented no remarkable features

"The pupillary margin of the upper leaf of the iris was in contact with the lens just ahead of the equator The lower pupillary border was entirely free of the lens and rested on apparently intact zonular fibers

"The ciliary body was flattened, especially the coronary portion The processes were somewhat elongated Scattered plasma cells were present Relatively normal and intact, but somewhat elongated, zonular fibers appeared to arise from the valleys both above and below"

The choroid, retina and vitreous were not remarkable

"Lens The lens measured about 6 mm anteroposteriorly at the equator A central area, 2.5 mm in diameter, representing the axial portion, was reduced to a membranous band about 0.5 mm thick, composed anteriorly of an intact folded glass membrane A wavy glass membrane could be followed along the posterior

surface from each outer margin but appeared to be absent or poorly formed centrally. Enclosed between these two membranes was a groundwork of a pale eosinophilic, slightly fibrillar mass, in which could be found fusiform cells occurring in clumps of three or four or singly, with pale blue nuclei and rather plentiful eosinophilic cytoplasm. Mitoses were not seen, but occasional groups of cells had so little cytoplasmic delineation as to suggest more than a single nucleus per cell. These cells were all separated from each glass membrane. The eosinophilic cytoplasm in places resembled that of normal lens fiber material. Some of this showed vacuolation.

"The doughnut-like portions of the lens measured about 2.5 by 1.5 mm in diameter above and 2 by 1 mm below, the shortest measurement being antero-posterior.

"Each fragment was covered by a normal-appearing capsule, with normally arranged epithelial cells anteriorly and normally inserting zonular fibers. The capsule folded together central to the previously described central patch.

"The central portion of the 'doughnut' itself was made up of recognizable lens fibers. The central regions, especially in the upper fragment, showed vacuolation and cataract formation.

"Recently proliferated lens fibers could be traced from equatorial cells and extended beneath the lens capsule. However, most of them terminated blindly with a swollen end adjacent to the anterior epithelium. A definite order was apparent in that the older proliferating fibers lying deeper ended nearer the beginning of the central patch."

#### SURGICAL TREATMENT OF DISK-SHAPED CATARACT

The surgical treatment of this type of cataract presents another interesting subject. The literature on this aspect of the problem is as yet meager. In my short experience I have found that more than one type of operation is needed, as the cataractous lens is composed of various parts, with distinct structures. A dissection exposing the existing lens substance to the solvent action of the aqueous should be the first operation. This also serves as an exploratory procedure in judging the consistency of the membrane, which on occasions can be torn apart or displaced. Collins,<sup>6</sup> in 1 case (that of an 18 month old child), was able to separate the central plaque. In both eyes it fell in the lower part of the anterior chamber and remained there, without any reaction. In most cases the membrane is firmly adherent to the rest of the lens and is too tough to be cut with an ordinary dissection needle, so that a stronger instrument must be used. In 2 of our patients (III 17 and IV 11) keratome incisions were made and the central membranes were cut with de Wecker scissors, leaving clear openings in both cases.

Total extraction should be considered with caution. In some cases of this type of cataract the central plaque is adherent to the hyaloid

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<sup>6</sup> Collins, E. T. Developmental Deformities of the Crystalline Lens, *Ophthalmoscope* 6: 577, 1908.

membrane, and extensive loss of vitreous can be produced as in the cases reported by Malbrán and Tosi.<sup>7</sup>

The special characteristics of these cataracts bring up for consideration the advisability of optical iridectomy. The periphery of the lens is clear, so that good visual results may be expected if the eye is otherwise normal. Improvement of vision after sufficient dilation of the pupil should give a hint as to the results to be expected from this operation. If the optical iridectomy proves efficient, it should prevent further surgical trauma, with the familiar picture of a severe reaction. Such a procedure, also, would prevent the inconveniences attendant on aphakia, including the use of strong convex glasses, which are disliked by most children. Fox<sup>2</sup> claimed good results with symmetric nasal iridectomies.

#### COMMENT

In the family under discussion, consisting of 59 persons, there were 22 males and 37 females. Fifteen of the members were dead, of those remaining, I have a more or less accurate history of 44. Thirteen have been examined. Of the entire 59, 16 are known to have congenital cataracts, but it is not known whether the 3 stillborn infants and the 2 infants who died shortly after birth were affected. Of the 16 members with congenital cataract, 5 were males and 11 females. Two cataractous fathers had 17 children, of whom 6 were affected. Three cataractous mothers had 13 children, of whom 5 were affected. In no case was cataract transmitted from father to son, in 6 cases the condition was transmitted from father to daughter, in 3 cases from mother to son and in 2 cases from mother to daughter. It may be noted that in the second generation the males had affected daughters only, whereas the females had affected sons, although this did not occur in the third generation and it probably happened by chance in the second generation.

So far the descent is direct, except for the first generation, in which neither parent had cataract. No cataract is known to have developed later in life in the unaffected members of this family.

Interesting speculations arise as to the type of heredity in relation to Mendel's laws, even though it is difficult to fit human pedigrees into such laws, especially when they are very short, as was this one. A study of the family tree shows that the transmission has been direct in every instance and that the condition has appeared regularly in the family from the second generation. The members who were not affected had no descendants with cataract. These facts are in favor of a "dominant" type of transmission, but since a dominant character requires

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<sup>7</sup> Malbrán, J., and Tosi, B. Catarata anular congénita, Arch de oftal de Buenos Aires 15 543 (Nov.) 1940.

only a single representative to become apparent, one of the parents (in generation I) should have had cataract. However, the presence of the condition in these persons has been denied repeatedly by my informants, and this one fact is against the dominant type of inheritance. If one were to conjecture that this transmission is of the recessive type, one would have to assume that the parents (generation I) were "carriers", their offspring, however, were affected in a number over the 25 per cent to be expected for the recessive type. Since both of the pair of genes must carry the recessive trait before the characteristic becomes manifest, the affected members must have mated in every instance with persons carrying the same character if the trait were recessive. This is unlikely, especially since no intermarriages have occurred. These facts, as well as the direct and continuous transmission of the defect, are strongly against the recessive type of inheritance. The rule "once free, always free" required by mendelism for a dominant character seems to hold good so far in this degree. Therefore, most of the facts are in favor of a dominant heredity. If the information given about the absence of cataract in the ancestors is reliable, one can regard this defect as a mutation which having once appeared is being transmitted as a dominant. One might surmise that the mutation occurred in the germ line of one parent during an early stage of development.

As to the heredity of the other anomaly present in the eyes examined, that is, the dislocation of the lenses, nothing can be said as yet, since the information on the presence of this condition in other members of the family is practically nil. I have found it in all the cataractous eyes, although this observation must be taken with caution in 2 of the cases (III 8 and III 11) since examination was made after repeated operations, which may have been the cause of the dislocation.

I hope that in the near future I shall be able to examine other members of this family, in order to shed light on several interesting problems. It must also be kept in mind that 8 members of generation III and all of generation IV are young and unmarried, in years to come, therefore, this family tree will probably grow in number and in interest.

From the foregoing observations, it would appear that the germ cell, male or female, is able to transmit to many members of many generations a well defined, and often almost identical, imperfection limited to a small part of the lens. The malign germinal influence, whatever it may be, acts on the lens at an early stage of the fetal development. The range of such influence must be very limited to damage only so small a portion of the body. This is emphasized when one considers that the weight of the normal human lens at 20 to 30 years of age is about 175 mg, or roughly three millionths of the usual body weight at that age.

Descriptions and illustrations of the cataracts found in the present cases place them in the "disk-shaped" type (Collins and Mayou<sup>8</sup>), or "ring" cataract (von Szily<sup>9</sup>). The literature on this type is scanty. In some of the reported cases the condition was discovered on pathologic examination, other cases were studied only clinically, with the exception of von Hess's case, in which the defect was first observed during life and later studied in sections. The first reference seems to be that of Becker (1883) cited by Collins<sup>6</sup> and Malbran and Tosi.<sup>7</sup> In his "Atlas" Becker described a case with characteristics resembling those of this type of cataract.

Another report is that of Vossius<sup>10</sup> (1893), the cataract in this case was found on pathologic examination in a blind eye with a dense central leukoma preventing clinical study. The eye was enucleated for cosmetic reasons, and the sections showed a cataractous lens with a central opaque portion enclosed between the anterior and the posterior capsule. No nucleus was present.

Collins<sup>11</sup> (1898) described a case of a lens with a central flattened zone in a paper dealing with anterior polar cataracts. At this time, as he admitted in a later paper,<sup>6</sup> he did not realize the significance of the flattened condition of the lens as evidence of lack of development of the nucleus. Such a lens was found in a buphthalmic eye of a 7 year old girl after enucleation. Its condition could not be made out clinically.

The next report was that of von Hess<sup>12</sup> (1905). His patient was first seen when 10 months old and had an iridectomy performed on both eyes. Clinically, there were a dense white central opacity of the lens, with diffuse cloudiness around it, and a clear periphery. The patient died at the age of 17, and Hess obtained the eyes three hours after death. Examination showed flattened, small lenses, in the thickest portion they measured only 2.5 mm, and in the center, 0.5 mm, the shape being similar to that of a red blood cell. The central portion was formed by the anterior and posterior capsules, both of which were wrinkled, with proliferated epithelium between. The

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8 Collins, E. T., and Mayou, M. S. *Disc-Shaped Cataract*, in *Pathology and Bacteriology of the Eye*, ed 2, Philadelphia, P. Blakiston's Sons & Co., 1925, p. 49.

9 von Szily, A. *Ueber angeborene familiäre "Ringstarlinse" nebst Hinweisen auf ihre Entstehung*, *Klin. Monatsbl. f. Augenh.* **81** 145 (Aug. 31) 1928.

10 Vossius, A. *Zur Kasuistik der angeborenen Anomalien des Auges*, *Beitr. z. Augenh.*, 1893, no. 9, p. 1.

11 Collins, E. T. *On the Pathogenesis of Anterior Polar Cataract*, *Tr. Ophth. Soc. U. Kingdom* **18** 124, 1897-1898.

12 von Hess. *Der Zentralstar*. *Pathologie und Therapie des Linsensystems*, in Graefe, A., and Saemisch, T. *Handbuch der gesamten Augenheilkunde*, ed 3, Leipzig, W. Engelmann, 1911, pt. 2, chap. 9, p. 196.

opacities around the central portion were of the zonular type, and the periphery was clear

After this case, I was unable to find any further reports until 1928, when von Szily<sup>9</sup> studied a family in which 4 members were affected with this rare type of cataract. The outstanding characteristic of all the lenses examined was, again, the absence of the central portions, which was replaced with an opaque membrane. The lens as a whole was like a ring in every instance. It was noted that the size of the central defect was about the same as the embryonic nucleus.

Another reference may be found in Vogt's<sup>13</sup> "Atlas" (figs 859 to 861), although the description is not as detailed as the previous ones.

Vázquez Barriére<sup>14</sup> reported a case in 1939 in which the lens was dislocated upward and nasally and was uniformly opaque, with just a few clear blebs. The center was similar to a 2 mm tunnel and was enclosed by an opaque membrane.

Malbrán and Tosi,<sup>7</sup> in 1940, reported the case of a 14 year old boy whose cataracts were noted shortly after birth. The lenses were dislocated nasally and upward. The authors described the lenses as formed by three portions, a clear peripheral one, a central thin, opaque zone, roughly diamond-shaped, and an intermediate zone between the two, less opaque and thicker than the center, so that the lenses had the form of a life-belt. Both these eyes were operated on. An intracapsular extraction was intended, but the capsule broke. The central zone seemed to be adherent to the hyaloid membrane, which was ruptured by the traction, with loss of vitreous. Pathologic examination of the specimens confirmed the clinical diagnosis of the type of cataract.

As to the type of developmental disturbance, congenital cataract has been considered as due to "arrest" in development, but, as Mann<sup>15</sup> stated, the word "arrest" indicates that normal development has simply been held at some stage without proceeding along abnormal lines, whereas "aberration" means that the resulting structure does not resemble any normal stage, therefore, any congenital opacity must be regarded as an aberration, since the lens is transparent during its normal development.

Various theories have been evolved regarding the embryonic changes leading to this type of cataract.

Vossius<sup>10</sup> interpreted his case as due to a nutritional defect of the axial portion of the lens, secondary to perforation of a corneal ulcer.

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<sup>13</sup> Vogt, A. *Atlas der Spaltlampenmikroskopie des lebenden Auges*, Berlin, Julius Springer, 1921.

<sup>14</sup> Vázquez Barriére, A. *Catarata anular congénita* (Ringstarlinse, von Szily), *Arch de oftal de Buenos Aires* **14** 875 (Oct) 1939.

<sup>15</sup> Mann, I. *Developmental Abnormalities of the Eye*, London, Cambridge University Press, 1937, pp 340 and 359.

Van Hess<sup>12</sup> concluded that this anomaly was probably due to a disturbance in the separation of the lens vesicle, and he classified this cataract as congenital, stationary and "central"

Collins,<sup>6</sup> in his interesting communication on the developmental deformities of the crystalline lens, reviewed the different stages of development in an attempt to place the time and type of disturbance leading to this anomaly. Before the lens vesicle has become completely closed anteriorly, the cells which form the posterior layer elongate and continue to do so after the vesicle is complete, filling its cavity. These are the primary fibers, which later are surrounded by others laid on at the sides and form the nucleus of the lens. If the cells forming the posterior layer for some reason fail to elongate and become transformed into fibers, the nucleus will not be formed, so that the laterally developed fibers will have nothing to encircle. The failure of development of the nucleus does not check the activity of the cells lining the anterior and lateral parts. The central mass results from the proliferation of the cells lining the anterior capsule, probably as an outcome of a low intracapsular pressure. The secondary fibers, having no nucleus to surround, form accumulations at the sides of the anterior mass, with irregularities and vacuolations.

Von Szily,<sup>16</sup> on the basis of his studies of congenital disturbances of the lens, explained the embryology of this type of cataract somewhat differently. The importance of these studies resides in the proof that in all the genuine "idiokinetic" malformations (that is to say hereditary malformations) "divergence from normal morphology is primary and disintegration of lens substance secondary." The opposite occurs in those forms of cataract in which the opacities affect a lens of normal structure. Injuries of diverse sorts, acting even in the very earliest stages of development, produce a primary disintegration with secondary morphologic disturbance.

On the basis of this theory, von Szily stated that "ring" cataracts can be attributed to a secondary disintegration of the whole thickness of the central portion of the lens, following "idiokinetic" disturbances in the normal delimitation of the two main sections of the embryonic lens, namely, the epithelium and the fibers. The nucleus is resorbed, so that the anterior capsule, together with epithelium, meets the posterior capsule, thus forming the central membrane. The enclosed remains of the lens epithelium is inclined to proliferation, so the membrane may become similar to capsular cataract.

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16 von Szily, A. (a) Kernschwund orden die soz "Ringstarlinse," in Henke, F., and Lubarsch, O. *Handbuch der speziellen pathologischen Anatomie und Histologie*, Berlin, Julius Springer, 1937, vol 9, pt 3, p 82, (b) Doyné Memorial Lecture. Contribution of Pathological Examinations to Elucidation of the Problems of Cataract, *Tr Ophth Soc U Kingdom* (pt 2) 58 595, 1938

According to most authors, this malformation is bilateral and hereditary, however, it is admitted that similar pictures may be found as secondary changes of other intraocular processes. Von Szily stated that such changes can be distinguished from typical disk-shaped cataract in that the ring is not always closed and the central membrane contains some fiber material. In the present cases, the presence of bilateral, congenital, hereditary cataract places the lesion with the genuine disk-shaped type, that is, one due to idiokinetic, rather than local ocular, disturbances.

“Ring” cataract may occur in otherwise normal eyes or may be associated with other abnormalities, such as aplasia or hypoplasia of the fovea, an occurrence explaining the poor vision obtained even after a good pupillary opening has been made or after dilation of the pupil, with exposure of the clear margin.

The association of disk-shaped cataract and dislocation of the lens is not infrequent, as can be seen in the description of the cataractous eyes we have examined and in the cases reported by von Szily,<sup>9</sup> Vázquez Barriére<sup>14</sup> and Malbrán and Tosi.<sup>7</sup>

Von Szily<sup>16b</sup> expressed the belief that if the cataract persists for a long time the central defect may become larger, owing to a secondary resorption phenomenon. In 1 of the present cases (II 9) the central portion of the right lens was filled with a flocculent material (as though a dissection had been performed). One wonders whether this could be explained by the resorption phenomenon just mentioned.

Regarding the other anomaly found in the reported cases, namely, the dislocated lenses, it can in all probability be designated as “ectopia lentis,” as it has all the characteristics described for this condition: congenital, hereditary, bilateral and symmetric. The displacement in these cases belongs also to the most common type, that is, upward and nasally.

Although ectopia lentis as a rule has a distinct hereditary tendency, sporadic cases have been described by Bell (cited by Mann<sup>15</sup>) and even cases of unilateral occurrence, by Parsons (cited by Mann<sup>15</sup>). It may occur exclusively in females or males but usually has no sex predominance.

From its hereditary and bilateral character, ectopia falls into a different group than coloboma despite the fact that irregularities and notches can be found in the edges of the ectopic lens. The zonule, however, is not so often absent in ectopia as in coloboma. The defect seems to be due to actual dislocation rather than to failure of development. The embryologic features of this condition are not well established as yet. When it appears as an isolated character, there is no evidence of primary abnormality of any structure but the zonule. It



appears to have no connection with coloboma or persistence of capsulopupillary vessels. It is probably an irregularity in the length and strength of the fibers, which causes the lens to be pulled toward the strongest ones. Since the dislocation occurs most commonly upward, weakening of the inferior zonular fibers is revealed. Regarding this fact Mann<sup>15</sup> stated: "If the zonule fibers are going to fail, they are more likely to do so in the lower part, which (being the unstable region of the fissure) is always most likely to show underdevelopment."

This explanation regards ectopia lentis as due to a defect limited to ectodermal structures, but the fact that anomalies of the iris, such as corectopia, polycoria and persistent pupillary membrane, are found in pedigrees showing ectopia cannot be overlooked. In 2 members of the reported family (III 16 and IV 14) I have found persistent pupillary membranes as an isolated character.

#### SUMMARY

A family of 59 members, representing four generations, is reported on. Sixteen of them had congenital cataracts. There were no known cases of this condition in the generations preceding the four reported on here.

All the members examined presented the type of cataract known as "disk-shaped," or "ring," characterized by the absence of the lens nucleus. This is due either to a failure of development of the primary fibers (Collins) or to a secondary resorption of the central parts, following an idiokinetic disturbance at an early stage (von Szily). This suggests the presence of genes controlling the development of the nucleus. Apparently, such genes are dominant.

Association of these cataracts with ectopia lentis was found in all the patients examined. No other local or systemic anomaly was present.

Members of the Department of Ophthalmology, Stanford University School of Medicine, and of the Laboratory of Ophthalmic Pathology, University of California Medical School, gave help in the preparation of this paper.

## Correspondence

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REVIEW OF AN OLD BOOK CONSERVATION OF VISION, J G A CHEVALLIER,  
PARIS, 1812

*To the Editor* —The author, Chevallier, was not a physician but a civil engineer. He seems to have known quite a bit about optics but was mostly interested in the practical side of his craft. In those days glasses were not prescribed by physicians, and he was probably the first reputable and learned optician to practice in Paris. He always had an eye to commerce and often blew his own horn, a characteristic which may be justified when one compares him with his colleagues of that day.

The second half of the book is of no great interest to ophthalmologists. It gives a description of various optical instruments, such as telescopes, mirrors and microscopes. The first half deals with the eye and with glasses. There is nothing one can learn today in these two hundred pages, but, as is often the case in old books, one finds amusing things—and now and then one is surprised by an accurate statement.

First comes a short chapter on the anatomy of the eye, then a rapid survey of the pathology of the eye. This book, being meant for the lay public, and the eventual purchaser of glasses, is written neither by nor for the medical profession, but it makes amusing reading, and this work of vulgarization is not bad.

Chevallier states, for instance, that squint should be treated early and advises occlusion against the amblyopia of squint. Strangely enough, he states that the oblique muscles are the real cause of strabismus.

The author mentions that cataract is often found among persons engaged in occupations in which they constantly face a strong fire, and this clinical remark reminds one of the injurious effect ascribed at present to infra-red rays. He is less fortunate in stating that cataract can be the cause of the central scotoma.

There are some interesting pages on the first contact with the outside world of patients operated on late in life for congenital cataract. These observations are similar to those made in more recent times, i. e., that the patient must control his new sensation by touch and that at first everything seems to be very near, and almost in contact with his eyes.

There is a fairly good description of keratoconus, but extraction of the lens is advocated.

Chevallier mentions the importance of a correct pupillary distance for glasses, but, of course, not because of any esophoria or exophoria. What he stresses is that one should look only through the center of a lens, as the periphery shows aberration.

He mentions Wollaston's periscopic lenses and understands clearly their qualities. However, he seems mostly to have manufactured bispherical lenses. Bifocal lenses of the Franklin type were known to him.

Blue glasses are rightly considered as "cool"

There is some general good advice on the hygiene of the eye, for example, one is pleased and surprised to read that one (in 1820) should sleep with an open window to have more air

It would be interesting to know how he chose the glasses for his patients, but he does not go into that. It seems to have been a sort of Donders method, by trial, starting from a chart, which he prints, giving the most usual glasses for a given age. (He evidently dealt especially with presbyopia, although he also gave concave lenses for myopia. Cylinders were, of course, unknown to him)

Much of his optical business was done by mail. He usually sent three pairs of glasses, and the patient chose the best.

Chevallier ground his own glasses and tells how

EDWARD HARTMANN, Paris, France

## News and Notes

EDITED BY DR W L BENEDICT

### GENERAL NEWS

**Summer Graduate Course in Ophthalmology, University of Rochester School of Medicine and Dentistry**—The Fourteenth Summer Graduate Course in Ophthalmology, under the auspices of the University of Rochester School of Medicine and Dentistry, will be held on August 5, 6, 7 and 8, 1946

The subjects of lectures and guest speakers follow: "Differential Diagnosis of Paralysis of Vertically Acting Muscles" and "Clinical Problems," Dr Francis H Adler, "Anomalies of the Fundus" and "The Fundus in Myopia," Dr Arthur J Bedell, "Slit Lamp Microscopy," Dr Harvey E Thorpe, "The Measurement of Strabismus" and "The Management of Strabismus in Children," Dr Maynard C Wheeler, "Herpes Simplex Cornea," "Herpes Zoster Cornea," "Experiences with Unusual Corneal Diseases" and "Ophthalmologic Problems Met at Morocco," Dr Trygve Gunderson, "Physiologic Optics in Refraction," Mr Frederick W Jobe, "Everyday Spectacle Problems," Mr Irving Lueck, "Ophthalmic Surgery," Dr J S Guyton, "External Diseases of the Eye" and "The Management of Dacryocystitis," Dr Ralph O Rychener, "Ophthalmic Research in the Navy," Alexander E MacDonald. On the final day there will be a surgical clinic at the Strong Memorial Hospital and a visit to the Bausch & Lomb factory.

**Training Course at Rochester Orthoptic Center**—The Rochester (N Y) Orthoptic Center is receiving applications for its next training course for orthoptic technicians. This course is accredited by the American Orthoptic Council. Information may be received from the Rochester Orthoptic Center, 208 North Goodman Street, Rochester 7, N Y.

# Abstracts from Current Literature

EDITED BY DR WILLIAM ZENTMAYER

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## Cornea and Sclera

TREATMENT OF SEPTIC ULCER OF THE CORNEA BY LOCAL APPLICATIONS OF PENICILLIN F JULER and M Y YOUNG, Brit J OPTH 29:312 (June) 1945

No attempt was made in this series to evaluate the effect of intramuscular administration of penicillin. The product was applied by local methods only.

The number of ulcers treated was 23, 2 of which occurred in the same eye, with an interval of one month between their appearances. The ages of the patients affected were distributed as follows:

Seven were over 60 years of age, of these, 4 did excellently, and 3 did well. Seven were between 50 and 60 years of age, 1 did badly, 3 did excellently and 2 did poorly. Seven were between 40 and 49 years of age, 2 did well and 5 excellently. One was 35 years of age and did not react to penicillin—the infecting organism was *Bacillus pyocyaneus*. One was 14 years of age and reacted excellently.

The solution used was sodium penicillate in a strength of 500 units per cubic centimeter. Two drops of the solution was instilled in the lower conjunctiva or, if possible, on the cornea itself. After several seconds the instillation was repeated. This procedure was carried out hourly by day and every two hours by night until the condition was obviously under control, when longer intervals were permitted. Atropine sulfate was used three or four times daily. The Saemisch section is advocated in cases of serious lesions. W ZENTMAYER

## General

OPHTHALMIC WORK IN A BRITISH GENERAL HOSPITAL IN NORTH AFRICA A J CAMERON, Brit J Opth 29:26 (Jan) 1945

This interesting article does not lend itself to satisfactory abstraction. The nature of the cases is described, and a number of unusual injuries, including foreign bodies in the eye, the orbit and the adnexa, are described. A large percentage of intraocular foreign bodies were nonmagnetic. Mortar fragments were preeminently the cause of wounds.

The opinion is expressed that myopic persons in subtropical countries tend with a definitely less strong lens to get as good vision as they previously had and that men with low myopia who required a correction to obtain vision of 6/9 or better could read 6/6 easily without correction. The author offers no scientific explanation of this observation but thinks the reason might be partly that the bright light produces a smaller pupil or that these men had become accustomed to gazing into the wide open spaces and leading an outdoor life. W ZENTMAYER

## General Diseases

PERIARTERITIS NODOSA AFFECTING THE EYE R SAMPSON, Brit J Ophth 29: 282 (June) 1945

An airman aged 20 years was admitted to a hospital with generalized clonic convulsions, followed by unconsciousness lasting several hours. Increasing anemia and emaciation with failure of the left ventricle resulted in death, after an illness of three months. Pathologic examination demonstrated well marked periarteritis affecting arteries in all systems, particularly the coronary arteries. Ophthalmoscopic examination made four weeks before death showed in the right eye retinal vessels of normal caliber and generalized retinal edema, more marked on the temporal half of the fundus, with blurred margins of the disk. Lateral to and above the level of the macula were several areas of retinal detachment of small extent, and deep to the retina in these areas were grayish white, branching nodules, somewhat resembling miliary tubercles of the choroid. In the left eye there was a large globular, exudative detachment of the retina, with no holes or tears. A week before death the fundi looked normal except that there were small, lightly pigmented scars at the sites of the choroidal lesions previously noted. No sign of albuminuric retinopathy was present. The eyes and the orbital contents were obtained for examination. The main interest lies in the presence of healed arteritis in many of the choroidal vessels. Similar appearances were in evidence in the retinal vessels in the disk of the right eye and in some of the extrascleral vessels.

W ZENTMAYER

## Injuries

SURGICAL APPROACH IN TREATMENT OF PENETRATING INJURIES OF SCLERA IN REGION OF CILIARY BODY J KOPP, Vestnik oftal 23: 18, 1944

Kopp gives a thorough analysis of his vast experience in treating injuries of the region of the ciliary body in both civilian and military cases.

In cases of injuries of the ciliary body the important factor is the secondary infection, the most painstaking care of the wound is therefore imperative.

The anesthesia should be adequate. No speculum should be employed, and sutures of the lid should be used instead, sometimes it is necessary to place sutures on some of the rectus muscles. If the patient is seen soon after the injury, the prolapsed vitreous is cut off, and the prolapsed ciliary body is put back in place. If the patient is seen a few days after the injury, the prolapsed ciliary body should be excised. Sometimes the ciliary body is pressed back with a spatula while the scleral sutures are being tied. Kopp applies scleral sutures in cases of gaping wounds only, while in cases in which the scleral edges are in apposition he uses conjunctival sutures.

In 11 cases of penetrating injuries of the ciliary body with intra-ocular foreign bodies, one eye was lost because of iridocyclitis and another because of purulent infection. The foreign bodies were extracted by the diasceral method according to the localization of the

foreign body In 19 cases of penetrating injuries of the sclera and ciliary body without intraocular foreign bodies, 10 eyes had to be eviscerated because of panophthalmitis, and 2 had to be enucleated because of iridocyclitis In the remaining 7 cases the results were as good as with any injury of the eye

Analysis of 30 cases of penetrating injuries of the region of the ciliary body in wartime shows that the same approach can be used as in management of industrial traumas In 12 of these cases there were exudates in the vitreous but only 4 eyes had to be enucleated In 18 cases the prolapsed ciliary body was excised and scleral sutures were applied, only 4 eyes had to be removed because of severe iridocyclitis Most of these patients came under observation several day after the injury

Kopp concludes that injuries of the region of the ciliary body should be treated with all possible speed and that most of the eyes can be saved if seen shortly after the injury

O SITCHEVSKA

#### PURULENT MENINGITIS AND DEATH FOLLOWING AN OCULAR INJURY REPORT OF A CASE L ZATZ, Vestnik oftal 23:47, 1944

A soldier received an injury of the left eye from a fragment of a mine The eye was enucleated at a front line hospital, and recovery was uneventful, but after a time meningeal signs appeared rigidity of the neck, a bilateral Kernig sign and absence of knee reflexes The spinal fluid showed the picture of purulent meningitis Sulfanilamide was given intravenously and intraspinally, but despite this therapy the patient died Autopsy showed a blind penetrating injury of the skull, the basal bone and the frontal lobe of the brain, there were abscess of the frontal lobe, basal purulent meningitis and an intracranial foreign body measuring 12 by 8 mm

Zatz therefore makes a plea for a routine roentgenographic examination in cases of crushing injuries of the eye, as well as a neurologic study, in order to avoid such a tragic result

O SITCHEVSKA

#### Lacrimal Apparatus

"DACRYORHINOPLASTY" A BLERAS GARCIA, Arch Soc oftal hispano-am 4:26 (Jan-Feb) 1944

When the operation of dacryocystorhinostomy fails or is not suitable, either of two new procedures can be made use of Arruga's operation (canaliculorhinostomy) and the operation of "dacryorhinostomy" The latter operation is in some respects like the one described by the author dacryorhinoplasty In 80 per cent of 200 cases in which Casanellos used the new technic the operation was successful Bleras Garcia, without knowledge of the work of Casanellos, was at the same time experimenting on the cadaver with the same procedure Three cases in which he performed the operation, with good results in 2, are reported

Mucous membrane from the lip was used for the graft. Two quadrilateral grafts were cut, one was sutured to the posterior border of incisions in the conjunctival mucous membrane, and the other, to

the anterior border. In this way a passage from the lacus lacrimalis to the interior of the nose was established. The technic of the operation is described in detail. This procedure was successful in the human subject.

H. F. CARRASQUILLO

### Neurology

VISUAL DISTURBANCES PRODUCED BY BILATERAL LESIONS OF THE OCCIPITAL LOBES WITH CENTRAL SCOTOMAS. M. B. BENDER and L. T. FURLOW, *Arch Neurol & Psychiat* 53:165 (March) 1945

The authors report in detail a case of bilateral lesion of the occipital lobe, describing and discussing the clinical picture from the time of injury throughout the period of recovery. After the patient had been completely amaurotic, vision returned in the peripheral fields, and restitution continued to take place medially, terminating in bilateral large central scotomas. During the period of recovery he had good perception of motion, defective color vision, little appreciation of form and ability to see best in the dark or in low illumination, all visual functions characteristic of the peripheral portions of the retina (in this case the peripheral "cortical retina").

The patient also manifested (a) the normal mechanism of psychologic filling in of visual field defects, thus perceiving objects as a whole, (b) retention of his psychologic field of vision about a subjective central point in a blind area, which made it difficult for him to realize that his central vision was lost, (c) reorganization of his psychologic field of vision when a new functional fovea was formed, (d) entoptic phenomena, with visualization of emanating "waves," and (e) fluctuation of perception in the remaining field of vision.

Opticomotor nystagmus was induced by having a striped drum revolve in his peripheral, but not in his central, fields of vision. Five months after the injury after-imagery could not be elicited with a light stimulus placed in any part of the field of vision.

S. R. IRVINE

HEMIFACIAL SPASM. REVIEW OF ONE HUNDRED AND SIX CASES. G. EHNI and H. WOLTMAN, *Arch Neurol & Psychiat* 53:205 (March) 1945

The records of 663 patients seen at the Mayo Clinic for various unwonted movements of the face were reviewed by the authors, of these, 106 had cryptogenic hemifacial spasm. The report excludes cases in which there was evidence of a gross pathologic lesion in the posterior fossa or the peripheral course of the facial nerve.

The following conclusions are drawn:

1. Women are more often afflicted than men, in the ratio of about 6 to 4.

2. Children do not have hemifacial spasm.

3. Encephalitic illnesses or arteriosclerosis, with or without hypertension, seldom bears a causal relation to hemifacial spasm.

4. The spasms usually begin in the orbicular oculi muscle on one side and slowly progress to adjacent muscles until, in certain cases, the entire facial musculature is involved.

For 7 patients the authors have no definite information as to the exact location of onset of the twitching. In all but 9 of the remaining 99 patients the muscles of the eyelids were involved early. Sixty-nine patients described their spasm as beginning in the eyelids, 7 patients in the upper lid, and 18 patients, in the lower lid alone, while in 21 patients the involvement ranged from the eyelids and "quivering in the ear drum" to twitching of the whole side of the face. The reason for the high incidence of early involvement of the lids is not known. Gowers explained the proneness to spasm in the orbicularis oculi muscle by saying that the "motor mechanism of this muscle is more sensitive, in consequence of its energetic reflex action." Oppenheim and other authors accepted this explanation without modification. In 9 of the patients the spasms did not start in the eyelids, and in 2 of these persons the lids never became involved.

5 Spontaneous remissions for periods up to three years have been noted.

6 The spasms in almost every case were aggravated by circumstances causing nervousness, fatigue or voluntary movements of the face.

7 No patient was able to stop the spasm by an exercise of the will.

8 Only 5 patients were seemingly cured without resort to surgical treatment, and in 3 of these the disturbance may well be in a period of remission.

9 Spino-facial anastomosis was performed on 3 patients, with satisfactory results in all.

10 There is evidence for the view that the lesion causing this condition is in the facial nucleus or the proximal portion of the facial nerve.

S R IRVINE

SYNKINETIC PUPILLARY PHENOMENA AND THE ARGYLL ROBERTSON PUPIL M D BENDER, *Arch Neurol & Psychiat* 53:418 (June) 1945

The author describes a case of skull fracture and complete paralysis of the right oculomotor nerve following a fall. The case is one of oculomotor ophthalmoplegia from which there was rapid but incomplete recovery, with iridoparesis and associated synkinetic phenomena as residua. On contraction of any of the formerly paralytic extraocular muscles, especially the inferior rectus, the sphincter of the right pupil contracted simultaneously. If this pupil were examined only for the conventional reactions to light and in convergence, the clinical picture would simulate the Argyll Robertson pupil. Another interesting feature of this case was the synkinetic contraction of the ciliary muscle in association with action of any of the formerly ophthalmoplegic muscles.

A second case is reviewed in which skull fracture was followed by blindness of the left eye, inability to raise either eyelid and paralysis of all movements in both eyes except abduction of the right eye. This case is another instance of recovery from oculomotor ophthalmoplegia with residual paralysis to stimulation with light and synkinetic constriction of the pupils. Were it not for the pupillary contractions associated with ocular movement other than convergence, the clinical



picture would strongly simulate the syndrome described by Argyll Robertson. It is interesting and significant that in this case, and in the preceding case, practically all the formerly paralyzed external ocular muscles recovered. Only the sphincter pupillae remained paretic, being inactive to light but contracting in association with movements of the eyes.

A third case is reported with signs of paralysis of the third, fourth and fifth cranial nerves on the left side. The causative factor was syphilis. After improvement with treatment, the left pupil would have been classified as the Argyll Robertson type were it not for the synkinetic phenomena, apparent not only in the sphincter pupillae but also in the superior eyelid. The retraction of the eyelid in association with ocular movements has been called the pseudo-Graefe phenomenon.

The details of 4 animal experiments are given. The phenomena of synkinetic pupillary constriction and retraction of the eyelid were produced experimentally in the monkey by intracranial section of the oculomotor nerve. These phenomena are partly explained by the theory of indiscriminate regeneration of oculomotor nerve fibers. It is concluded that the so-called, or pseudo, Argyll Robertson pupil, sometimes noted after head injury with complicating oculomotor ophthalmoplegia, has no etiologic relationship to the classic pupillary reaction originally described by Argyll Robertson.

S R IRVINE

#### BRANCH THROMBOSIS OF MIDDLE CEREBRAL ARTERY K C WYBAR, Brit J Ophth 29: 355 (July) 1945

A middle-aged woman suddenly experienced left-sided headache associated with a defect of the right side of both visual fields. There was transient aphasia of the receptive type with disturbance of comprehension of written speech and with a slight jargon aphasia.

The visual agnosia, which is the only persistent feature, is a right superior homonymous quadrantic scotoma adjacent to the fixation point with sharply defined vertical and horizontal borders. The peripheral border, which was at first vague, is now more decided. There is incongruity between the scotomas, the left one being larger than the right.

The clinical picture is in agreement with a diagnosis of thrombosis of the parietotemporal branch of the left middle cerebral artery.

W ZENTMAYER

#### Ocular Muscles

#### HEREDITY AS A FACTOR IN SQUINT L P DARR, Am J Ophth 28: 898 (Aug) 1945

Darr refers to various authorities and concludes that heredity may be a factor in squint and that it should be watched for in families in which it has occurred.

W S REESE

#### DIVERGENCE PARALYSIS AND HEAD TRAUMA N SAVITSKY and M J MADONICK, Arch Neurol & Psychiat 53: 135 (Feb) 1945

The authors report 6 cases of divergence paralysis encountered in a series of 1,550 personally observed cases of head injury. Only

5 similar instances were found among 17,783 cases of head injury reviewed in the literature, perhaps because the patients are often too ill to be tested or because careful examinations are not made to determine its presence. The authors are of the opinion that there is insufficient proof that this condition can occur on a hysterical basis and that the head trauma causes injury to the hypothetic center for divergence in the midbrain. In some cases the complaint persisted so long (up to five years after injury) that the lesion could be considered irreversible, perhaps a laceration.

S R IRVINE

### Trachoma

TRACHOMA IN WEST AFRICAN NEGROES J G SCOTT, Brit J Ophth  
29: 244 (May) 1945

The purpose of the paper is to assess the rate of infection among Negroes in British West Africa and to describe the disease as it affects the natives.

Trachoma of the West Coast African Negro is a mild disease. It is of the general infiltrative type. It affects 5 per cent of school children, 10 per cent of soldiers and 25 per cent of population in some villages in the Gambia. The same disease is found in 10 per cent of soldiers on the Gold Coast, in 10 per cent of Nigerian soldiers and in 2 per cent of Cameroon soldiers. Three hundred American Negro soldiers had no similar infection but were not immune.

W ZENTMAYER

### Tumors

MALIGNANT PALPEBRAL TUMORS PEREZ-BUFIL, Arch Soc oftal hispano-am 4: 59 (Jan-Feb) 1944

Early surgical removal of malignant palpebral tumors and covering of the gap with lateral flaps are advocated by the author. He considers this treatment preferable to roentgenotherapy. Five cases are reported in which good results were obtained with respect to cure and cosmetic effects.

H F CARRASQUILLO

CHOLESTEATOMA OF THE ORBIT J BASTERRA, Arch Soc oftal hispano-am 4: 67 (Jan-Feb) 1944

The author reports a case of this rare condition, only 8 cases of which are recorded in the literature. The patient, a woman aged 49, complained of protrusion of the left eye. A tumor about the size of a cherry was observed between the upper orbital brim and the eyeball. The tumor was removed, and pathologic examination revealed "small masses formed by cellular detritus undergoing lipid degeneration."

A discussion of this tumor is given

H F CARRASQUILLO

RECURRENT GLIOMA OF THE RETINA TREATED BY CHAOUL'S METHOD OF ROENTGEN IRRADIATION C COSTA, Arch Soc oftal hispano-am 4: 72 (Jan-Feb) 1944

The left eye of a boy 1 year old was enucleated for a glioma. Five months later the tumor recurred in the orbit. Treatment was with

irradiation according to the method of Chaoul. This technic is considered better than the ordinary method of roentgen irradiation. One month later the tumor had disappeared entirely. Three months later, however, the growth reappeared. The child is still under treatment.

H. F. CARRASQUILLO

### Vitreous

SURGICAL TREATMENT OF HEMOPHTHALMOS. KAMINSKAYA, *Vestnik oftal* 23, 3, 1944

Kaminskaya treated surgically 25 patients with hemorrhages into the vitreous according to Nedden's method. The treatment consisted in withdrawal of from 0.2 to 0.6 cc. of vitreous by puncturing the sclera at a point 5 to 6 mm. below and temporal to the limbus. This procedure could be repeated two or three times at intervals of six weeks. No reaction was observed. Hypotony of the eye was observed for several days, but usually the tension became normal afterward. Vision was increased to a considerable degree in a few patients. Kaminskaya recommends this method as the most effective and at the same time the simplest. It was particularly useful in treatment of wartime victims of intraocular hemorrhages due to injuries.

O. SITCHEVSKA

### Therapeutics

INJECTION OF SULFONAMIDE COMPOUNDS INTO THE ANTERIOR CHAMBER. J. L. CASTILLO, *Arch. de oftal. de Buenos Aires* 19, 81 (Feb.) 1944

Although the concentration of sulfanilamide in the blood may be high, it is always lower in the intraocular tissues and fluids. With the idea of bringing to a higher level the concentration of this drug in the eye, the author introduced a 5 per cent solution directly into the anterior chamber after removal of the aqueous humor. The tolerance of the 4 patients subjected to the experiment was very good. The author suggests this method of administration for a more active and shorter course of therapy in cases of infectious processes of the cornea, anterior chamber and uvea.

H. F. CARRASQUILLO

LOCAL USE OF SULFONAMIDE COMPOUNDS FOR OCULAR DISEASES. E. SELFA, *Arch. Soc. oftal. hispano-am.* 3, 442 (Nov.-Dec.) 1943

The sulfonamide compounds may be used systemically or locally. For local use the author has used advantageously a 5 per cent solution of sodium sulfapyridine, 5 and 10 per cent solutions of sulfathiazole and a 5 to 25 per cent solution of sulfamethylthiazole. The drugs have been used locally with good results in treatment of acute pseudomembranous conjunctivitis occurring with whooping cough, phlyctenular conjunctivitis, gonococcal ophthalmia neonatorum, inclusion conjunctivitis of the newborn, and acute conjunctivitis produced by the staphylococcus, the Koch-Weeks bacillus or the pneumococcus, as well as in the conservative treatment of stricture of the lacrimal passages and as an application to the lids after operations for ectropion and trichiasis.

H. F. CARRASQUILLO

# Society Transactions

EDITED BY DR W L BENEDICT

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## SECOND PAN-AMERICAN CONGRESS OF OPHTHALMOLOGY

Conrad Berens, M D, New York

*Preliminary Report of Meeting at Montevideo, Uruguay, Nov 26-Dec 1, 1945*

Our Uruguayan colleagues were loyal hosts to the Second Pan-American Congress of Ophthalmology, which was held in Montevideo. It was encouraging to see such a splendid gathering of ophthalmologists of the Western Hemisphere so shortly after the cessation of international hostilities. Dr Vasquez Barrière, of Montevideo, president of the congress, opened the meeting, stressing inter-American cooperation for the advancement of ophthalmology and the prevention of blindness. He then presented a most illuminating history of ophthalmology in the Americas. In conclusion, Dr Vasquez Barrière stated that he was sure that this meeting of the Pan-American Congress of Ophthalmology marked a new stage in the ophthalmology of the Americas. He reminded those present of the great work of Dr Harry Gradle in establishing the Pan-American Congress of Ophthalmology and expressed deep regret that Dr Gradle was not able to be present.

This was a great loss to the meeting, and Dr Gradle's constructive presidential address was read by Prof Moacyr Alvaro, of Brazil. Dr Gradle wrote:

"This, the second meeting of the Pan-American Congress of Ophthalmology, marks an important epoch in the history of ophthalmology in the Americas. For two years this meeting has been postponed, not only because of travel conditions imposed by the war but even more because of the handicaps on science that unleashed brutality produces. But now we can gather in quiet and peace to describe and discuss how best we, the ophthalmologists of the Western Hemisphere, may aid our people. It is solely for that purpose that the Pan-American Congress of Ophthalmology exists.

"But a forum of this character must be more than merely a meeting place for the exchange of scientific ideas. To be of real value to all its members, there must be constructive aspects that will tend to advance the science of ophthalmology in all parts of the world inhabited by members of the Congress. The constructive phase of the society cannot be confined to the time of the meetings alone but must live with the members day by day. It must be a power, a force, the sole object of which is the advancement of the science of ophthalmology and to which the members can turn as necessary. Your officers of the Pan-American Congress of Ophthalmology are endeavoring to supply that force through *Ophthalmología Ibero Americana*, through the Kellogg Pan-American fellowships in ophthalmology and through the work of

the various committees, whose reports you are to hear within the next few days

"Through practical experience in the United States of America and in Brazil, it has been found that the most potent factor in the elevation of the standards of ophthalmology is the existence of a board for the purpose of setting standards and for the voluntary examination of men who wish to be recognized by their fellows as qualified in ophthalmology. To that end, I propose the development of a South American Board of Ophthalmology, dedicated to the elevation of the standards of training and of the practice of ophthalmology. Such a board should, of course, be an independent institution, originated by the educators in ophthalmology and supported by all the local and national ophthalmologic societies. Each country should be represented by elected representatives in the proportion of 1 to each hundred ophthalmologists in the country. The board should meet once a year and should determine which of the applicants from all the countries are eligible for examination. Then the examination should be determined on, and on his return home the examination should be given in each country by the elected representative, assisted by as many oculists as he may deem necessary. Only those candidates approved by the general board should be eligible for the examination. On successful completion of the examination, a certificate should be granted by the board, and eventually such certificate should be required for appointment to hospital or university positions.

"It is one of the greatest regrets of my life that I am unable to be with you for this meeting in person, but my thoughts and my hopes will be with you constantly. May your labors prove interesting and valuable, and may the fruits of your labors bring advancement in knowledge to world ophthalmology."

Dr Gradle's recommendation to form a board of ophthalmology for Latin America was later acted on and accepted.

Among the North American ophthalmologists who were present were Dr Thomas D Allen, of Chicago, Capt Clifford A Swanson, representing the United States Navy, Comdr Walter P Griffy, representing the United States Public Health Service, Dr Joseph I Pascal, of New York, Dr Ramon Castroviejo, representing the American Ophthalmological Society, Dr Conrad Berens, representing the American College of Surgeons, and Dr Paul Tisher, of New Britain, Conn.

The meeting offered an excellent opportunity to hear of the splendid work done in South America in the treatment of ocular diseases and in the prevention of blindness. Mrs Merrill the executive director of the National Society for the Prevention of Blindness, was hostess at a luncheon for representatives of all the countries participating in the congress. The progress in preventing blindness was described by each of the representatives.

One of the highlights of the meeting was Dr Arruga's arrival from Spain. It was unfortunate that his trip was delayed by storms, but it was stimulating to have him present even for a part of the meeting. His discussion of the treatment of detachment of the retina was based on his recent experiences and was a most valuable contribution to knowledge of this subject.

One of the important resolutions passed at the meeting was to change the name of the organization to the Pan-American Association of Ophthalmology. The officers of the association, elected at the Montevideo meeting, were as follows: president, Dr Harry S Gradle, honorary president, Prof Alberto Vasquez Barrière, vice presidents, Dr Francisco Belgeri (Argentina), Dr Frank Brawley (United States of America), Dr J Pereira Gomes (Brazil), Dr Frederick C Cordes (United States of America), Dr J A MacMillan (Canada), Dr Alexis Agüero (Costa Rica), Dr C Espinoza Luque (Chile), Dr R Pacheco Luna (Guatemala) and Dr A Torres Estrada (Mexico), executive secretaries, Prof Moacyr E Alvaro (Brazil) and Dr Conrad Berens (United States of America). Communications concerning the association should be addressed to Prof Moacyr E Alvaro (1151 Rua Consolação, São Paulo, Brasil), if mailed south of Panama, and to Dr Conrad Berens (301 East Fourteenth Street, New York 3), if mailed north of Panama.

The committee on ophthalmologic education appointed a president, Dr Jorge Valdeavellano (Lima, Peru), and three secretaries, whose work will be divided as follows: Dr Thomas D Allen (Chicago), in charge of Canada and the United States, Dr Miguel Branly (Cuba), in charge of Mexico, the continental countries of Central America, the Islands of the Caribbean, Venezuela and Colombia and Dr Raul Rodriguez Barrios (Montevideo, Uruguay), in charge of Ecuador, Peru, Bolivia, Chile, Argentina, Paraguay and Brazil.

The committee on Kellogg fellowships appointed Dr Harry S Gradle, Dr Conrad Berens, Dr Tomas Yanes and Prof Moacyr E. Alvaro to represent the association.

The committee appointed to draw up a constitution and by-laws for the association consist of Dr Tomas Yanes, Dr Conrad Berens and Prof Alberto Vasquez Barrière.

The scientific program was most instructive, and the proceedings will be published in a later issue of the ARCHIVES.

The next meeting of the association is planned for February 1948 in Habana, Cuba. Ophthalmologists in the Western Hemisphere will soon receive a communication inviting them to become members of the association and to participate in the work of this organization. Membership includes a subscription to the association's official publication *Ophthalmología Ibero Americana*.

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#### COLLEGE OF PHYSICIANS OF PHILADELPHIA, SECTION ON OPHTHALMOLOGY

Warren S Reese, M D, *Chairman*

George F J Kelly, M D, *Secretary*

Dec 20, 1945

#### Amblyopia Due to Dietary Deficiency: Report of Eight Cases. COMMANDER A D BEAM, USNR (by invitation)

Early in the spring of 1944 the United States Naval Hospital in Philadelphia was designated by the Surgeon General as the national center for the rehabilitation of blinded personnel of the Navy and the

Marine Corps Only men whose vision with correction is 20/200 or less in the better eye are admitted to this special service Up to the time of this report, 165 patients have been admitted Of these, 101 had suffered loss of vision as a result of traumatic injury, 29, as a result of methyl alcohol poisoning, and 27, after various ocular diseases The remaining 8 patients became blinded during their period of imprisonment under the Japanese It is this last group of patients with whom I am concerned in this report

All 8 men, with normal vision on enlistment, were captured at the fall of Corregidor Five of them were Marines and 3 sailors, only 1 of whom had sustained physical injury during the encounter prior to capture, and that was confined to the lower extremities They were all between the ages of 20 and 32 years Before capitulation, for five months, their living conditions had been far from satisfactory, and their diet had been rationed and steadily reduced After capture all 8 men survived the death march from Bilibid to Cabanatuan where 6 of them were imprisoned until the date of liberation, on Feb 4, 1945 The remaining 2 were later taken to Japan, after they had begun to have visual deficiency During their period of imprisonment all of them were forced to engage in strenuous physical labor and suffered the physical hardships of discipline now so well known to every one Loss of weight varied from 40 to 60 pounds (18 and 27 Kg) among the 8 men The diet during the entire period of incarceration was far below that specified by international law The average daily intake was 200 to 300 Gm of polished rice, or about 7 tablespoons, and a thin soup made with sweet potato vine, which was given about three times a week This constituted a diet of approximately 1,000 calories per day Occasionally the intake was greater or less, but this represents the usual food intake All these patients showed evidence of severe beriberi, and 7 of them had pellagra, of varying degrees of intensity Visual loss appeared in all of them, without other specific prodromes, and proceeded to the maximum deficiency in one to four weeks Blindness in all these prisoners developed between four and one half to eight months after capture Once the loss of sight was established, it remained static, even after they were freed and given various forms of therapy Loss of vision was painless in each instance, and except for the signs of dietary insufficiency there were no common factors that would suggest a toxic, infectious or traumatic cause In addition, 7 of the patients had bilateral nerve deafness, in which the hearing loss varied from 11 to 36 decibels Deafness was a concomitant feature of visual loss and was first noted at the onset of blindness or later All the 8 men had some evidence of peripheral neuritis, as did nearly all the other prisoners None of these men had symptoms of night blindness but, on the contrary, found that their vision was better during twilight or early evening Hypoproteinemias and occasional bouts of diarrhea were common to all the prisoners including those under discussion All these patients stated that there were many other prisoners who became blind in a similar manner but failed to survive the period of confinement for one reason or another

These 8 men with severely impaired vision present histories and physical signs which indicate that their visual loss probably resulted from dietary deficiency However the possible effect of some chemical

intoxication cannot be completely disregarded, even though there does not seem to be any common factor. The effect of a prolonged deficiency in diet on the visual sense of man during a period of strenuous and enforced labor has never been determined. Therefore, there may have been three groups of etiologic factors: deficiencies in such required elements as vitamins, minerals and proteins, intoxications of a chemical and bacterial nature, and the effect of strenuous physical activity with inadequate caloric intake. I am unable to state just what influence each of these factors had on the development of blindness in the circumstances just related, but from the endless array of published data it would appear that avitaminosis is the principal factor to consider. However, in discussing vitamin deficiencies, I do not intend to exclude the possible effects of other contributing factors or to indicate any assessment of their influence.

Only the vitamins usually thought to be concerned with the physiology of the eye will be considered, vitamin D being excluded.

*Vitamin A*—The minimum daily requirement of vitamin A is considered to be about 5,000 international units. The source of vitamin A in the diet of these men was limited to that contained in the thin soup made from vegetable leaves and water. None of these men suffered from night blindness, and only 2 showed evidence of corneal disease on admission to this hospital. One patient had had a perforating corneal ulcer in his right eye, whereas there were no opacities or history of inflammation of the left eye. On examination at this hospital, the lower two thirds of the cornea of the right eye was opaque and vascularized, and there was an anterior synechia. The left eye showed proliferation of the limbic vessels. One other patient had had "sore eyes" three months after capture. An American physician told him that he had corneal ulcers, these lesions became symptomless with no change in diet and with treatment limited to instillation of yellow mercuric oxide once a day. When this man was first examined here, there were seven or eight superficial opacities of each cornea associated with well marked proliferation of the limbic vessels. The corneal opacities were not dense, and there was little loss of corneal substance. These 2 cases may represent keratomalacia and xerosis of the cornea, respectively, although in neither was there evidence of conjunctival xerosis nor had the patients suffered from day blindness.

*Thiamine*—Thiamine, or vitamin B<sub>1</sub>, has been proved necessary in maintaining normal neurologic function. Inadequate ingestion, absorption or utilization of this heat-labile portion of the vitamin B complex causes the disease known as beriberi. The Committee on Nutrition of the National Research Council recommends between 1.5 and 2 mg. daily for a well balanced diet.

The rice which these men ate was chiefly polished. The polishing process, like the milling of flour, removes valuable constituents, notably the vitamins, protein and mineral elements. The discovery that a diet which consists solely of polished rice will produce beriberi gave an early incentive to the study of vitamins. Polished rice is practically devoid of all vitamins, but beriberi is due specifically to the lack of thiamine.

Each man in this group suffered symptoms of severe beriberi, including peripheral neuritis, edema of the extremities, weakness, anorexia



and diarrhea. Palpitation and shortness of breath were noticed by 3 of them. Massive doses of thiamine hydrochloride, given on their liberation in 1945, relieved all these symptoms, but the amblyopia which had occurred during the attack of beriberi was not improved. One patient received large doses of vitamin B complex seven months after his vision failed, when the Japanese selected a group of 100 prisoners all suffering from beriberi, half of whom were given vitamin therapy in addition to the usual diet, while the other half was maintained on the unfortified rice and soup diet. This man improved during this study with respect to his neuritis, edema and weakness, however, there was no change in his vision during or after the six weeks of the experiment.

On their admission to this service, the vision of these 8 men ranged from 1/200 to 10/200 in the better eye. Each had bilateral absolute central scotoma, which extended 5 to 12 degrees from the fixation point, and 2 also had bilateral concentric contraction of the peripheral fields. The pupils were semidilated and reacted sluggishly to light. The results of funduscopic examination were essentially normal except that each man showed evidence of bilateral atrophy of the optic nerve varying from well marked temporal pallor to advanced atrophy. The atrophy was of the primary, or descending, type. Treatment, consisting of a high vitamin diet supported by large doses of thiamine hydrochloride, has failed to cause any visual improvement in these patients. There is considerable evidence in the literature to support the theory that lack of thiamine in the diet may cause retrobulbar neuritis and optic nerve atrophy if the condition remains untreated. The dietary deficiency associated with chronic alcoholism is a classic example.

*Nicotinic Acid*—Pellagra is a disease of nutrition caused by deficiency in nicotinic acid (the P-P factor). Although other factors of the vitamin B complex may contribute to this disease, their significance is uncertain. Typical cases of pellagra are characterized by three groups of symptoms: a typical form of dermatitis, digestive disorders with or without diarrhea and psychoses of the confusional type. Typical signs of this disease occurred in 7 of the 8 patients presented here. The other patient apparently had no evidence of pellagra, even to the extent of glossitis, which is often one of the first signs of nicotinic acid deficiency. Although peripheral neuritis and atrophy of the optic nerve have been attributed to this disease (Wilkinson), it is probable that concomitant thiamine deficiency is the true etiologic factor. The occurrence of atrophy of the optic nerve and peripheral neuritis in the patient who presented no signs or symptoms of pellagra tends to support this belief. These men suffered no ocular change which it is thought can be directly attributed to nicotinic acid deficiency. Their pellagra healed soon after their liberation, when they received large doses of vitamin B complex.

*Riboflavin*—In 1940 Sydenstricker described the ocular effects of a riboflavin deficiency which included the symptoms of photophobia, sensations of roughness or burning of the eyelids and visual fatigue. The commonest sign was circumcorneal injection, often with invasion of the cornea by capillaries from the limbic plexus. Superficial corneal nebulas were also noted. These signs and symptoms responded favor-

ably to riboflavin therapy. Four men in this group gave a history of having had "sore eyes" and photophobia during their period of incarceration. Three of the 4 men exhibited definite proliferation of limbic vessels, and 1 showed superficial corneal opacities on examination here. The remaining men showed no evidence of proliferation of the limbic capillaries. Local areas of proliferation, usually traceable to an antecedent corneal inflammation, were not considered. Symptoms of photophobia and burning were relieved soon after liberation, when adequate vitamin therapy was instituted, but no change in the vascular proliferation has been noted during the past eight to ten weeks. A daily dose of 5 mg. of riboflavin has been administered daily since the patients arrived here.

*Vitamin C*—The ocular manifestations of vitamin C deficiency are probably limited to ocular hemorrhage in patients with scurvy. However, there is some evidence that cataract formation may be influenced by lack of this vitamin in the diet. Three of these patients were told that they had scurvy at one time or another while prisoners on Luzon. Their description of the cutaneous lesions is not typical, although their gums were swollen and bled easily. They gave no history of subcutaneous hemorrhage or bleeding except from the gums and nose. Examination here revealed no pathologic condition of the eyes attributable to vitamin C deficiency.

*Comment*—In this group of 8 men who became amblyopic while on an inadequate diet during imprisonment the outstanding pathologic change in the eyes common to all of them was the atrophy of the optic nerve, with central scotoma in each eye. Dietary deficiency, notably in thiamine, appears to have been the etiologic factor. Signs and symptoms of severe beriberi were present in each case, thus establishing proof of thiamine deficiency. Analysis of the diet, the bulk of which was polished rice, reveals little or no source of this vitamin. Rice contains 79.4 per cent carbohydrate, 7.6 per cent proteins and 0.3 per cent fat, which gave them a high carbohydrate diet. It has been well established that the thiamine requirement increases with the carbohydrate intake and with physical exertion. Ten hours of hard labor per day associated with a high carbohydrate diet increased the thiamine requirement. The need for thiamine was great and the source negligible. There is lack of evidence to support the influence of other avitaminoses on the amblyopia from which these patients suffer.

Again, no attempt has been made to evaluate the significance of other possible contributing factors due to dietary deficiency, intoxication or circumstances of existence such as were endured by these men. Only in highly controlled circumstances could such a study be of definite value. Certainly, these variable factors cannot be assessed in retrospect.

#### DISCUSSION

DR. WALTER I. LILLIE. Commander Beam has presented a series of patients with typical chronic retrobulbar neuritis and resulting simple atrophy of the optic nerve due to deficiency of the vitamin B complex in the diet. The patients were sailors and Marines who were prisoners of the Japanese. He has definitely shown that the condition was actually due to a deficiency of thiamine. I have seen similar cases at Valley Forge Military Hospital, in the Army personnel, so one can conclude

that all branches of the service under similar conditions are similarly affected. One of the sailors noticed that while he was on the polished rice diet his vision diminished but when he was fed the unpolished rice his vision improved. He always made an effort to obtain as much unpolished rice as possible.

In the treatment of these debilitated states due to dietary insufficiency, one must be careful in giving dextrose intravenously. If it is not fortified with vitamin B, it will utilize the remaining vitamin B in the body tissues and produce an added deleterious effect.

### **Method of Closing the Cataract Incision by Sliding a Large Conjunctival Flap from Above Down over a Corneoscleral Suture**

DR P H DECKER, Williamsport, Pa (by invitation)

This conjunctival flap will temporarily bury the corneoscleral suture and the entire incision. About the fourth or fifth day the conjunctival sutures spontaneously cut out, allowing the conjunctival flap to retract, thus automatically exposing the corneoscleral suture, which is removed about the tenth day.

The principle behind this procedure is that the corneoscleral suture gives adequate strength to closure of the incision, preventing loss of vitreous, while the conjunctival flap has an adequate sealing effect on the closure allowing rapid and early reformation of the anterior chamber. By combining the two procedures, namely, the corneoscleral suture and the large sliding conjunctival flap, both needed elements in closure of the incision are obtained that is, loss of vitreous is guarded against by the corneoscleral suture and delayed reformation of the anterior chamber, with its complications, is prevented by the conjunctival flap.

A film showing the operative procedure in 6 cases was presented.

### **DISCUSSION**

DR WILLIAM ZENTMAYER. In looking up the literature for Dr Decker, I found that this procedure had been employed by Kuhnt in cataract operations.

Kuhnt makes a large conjunctival flap, as described by Dr Decker, in addition he makes a horizontal incision well up in the cul-de-sac. The latter allows for greater freedom in bringing down the flap and, therefore, better coverage of the wound than can be obtained without that incision.

DR EDMUND B SPAETH. I had the pleasure of seeing Dr Decker's film with him at his home, so he knows, at least in part, what I am about to say, for we had a discussion at that time. It seems to me that he lays too much stress on the necessity for firm closure. His two lateral sutures with the sliding conjunctival flap will give this in all but extraordinary circumstances. At the same time the conjunctival flap should seal off the anterior chamber.

I agree with him as to the necessity of closing the anterior chamber promptly. For years I have used the conjunctival flap for closure in all cataract operations in one-eyed patients. Nonformation of the anterior chamber, if it continues for more than two or three days, can cause serious consequences. His beautiful film shows that without any possibility of difference of opinion, in a most conclusive manner.

DR JAMES S SHIPMAN. I also should like to congratulate Dr Decker on this beautiful presentation of an interesting subject. From

the pictures that he has shown I cannot see the necessity for using any suture. The way in which the cataracts were delivered and the way in which he kept his patient's eyes so still was beautiful to see. I should like to ask what kind of anesthesia he used. Every cataract operation that was shown was done skilfully and with little trauma. Certainly, so far as could be seen from the picture, there was no danger of immediate loss of vitreous.

The only excuse for a suture in this operation would be for his second reason, that of preventing delayed closure of the anterior chamber. In his technic, excellent as it was, I did not once see where he replaced the iris pillars. What happens to them? Was the pupil dilated with atropine or with homatropine? What drug was instilled at the first dressing? Was it atropine? To me these points are important and have a great deal to do with the closure of the anterior chamber. In my opinion, if the pillars are not replaced, they will be incarcerated to a certain degree and will lead to slow closure of the anterior chamber. I still believe that there is no necessity for using atropine for the first dressing when good intracapsular extraction has been performed, as was done in all these cases. Atropine is necessary in doing an extracapsular extraction, in which a good deal is involved, but with a complete intracapsular extraction there is no necessity for it. Certainly, there is no need of employing atropine until the anterior chamber has reformed, and it is my experience that the majority of them do reform within twenty-four to forty-eight hours after operation. A large conjunctival flap is a great help in getting the anterior chamber to reform, and it eliminates one of the objections to cataract extraction without a suture, *i. e.*, slow closure of the anterior chamber.

I have not come to believe that sutures are necessary for safe cataract extraction. I can do a better operation without them, and I do not use them except on rare occasions. I used one last week in an eye in which I knew there was vitreous in the wound, as the result of a basal iridectomy. The man was a poor patient, and I did not have his facial nerve blocked. Later, I had to remove the lens, and I felt that vitreous would present itself when I made the section. I enlarged the iridectomy incision slightly, then inserted three corneoscleral sutures before completing the section, but, in spite of this, vitreous is still seeping from the wound, ten days after extraction. I cannot be convinced that corneoscleral sutures or conjunctival sutures, such as Dr Spaeth described, will keep the vitreous in when it is going to escape. If vitreous is going to be lost, it will be, regardless of any suture. I still feel that a well made corneal section with a good conjunctival flap is the best operation for cataract extraction.

DR P H DECKER. I wish to thank Dr Shipman for his comments, but I still feel that sutures are necessary, at least in my hands. With regard to replacing the iris pillars, this is always done when there is any question of incarceration. I omitted this step in order to conserve film, however, I might add that I do not always insert an instrument into the anterior chamber after the extraction in order to replace an imaginary incarceration, as I feel that there is danger of inadvertently rupturing the hyaloid membrane with any unnecessary intraocular instrumentation after the extraction of the lens.

## Book Reviews

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**Physical Chemistry of Cells and Tissues** By Rudolf Hober, M D ,  
with the collaboration of David I Hitchcock, J B Bateman,  
David R Goddard and Wallace O Fenn Price, \$9 Pp 676,  
with 70 illustrations Philadelphia The Blakiston Company, 1945

Those who knew R Hober's standard work on the physical chemistry of cells and tissues looked forward with great expectation to the first edition in English This work has had six German editions between 1902 and 1926 and has been frequently called the bible of the physicochemistry of cells The expectations are amply fulfilled by the English edition, which is by no means a condensation of the former publications but is an entirely new book which covers the recent developments in the field of cellular physicochemistry In the introduction, selected principles of physical chemistry are presented by D L Hitchcock in a concise and clear form, similar to that of his book, "Physical Chemistry for Students of Biology and Medicine" (Springfield Ill Charles C Thomas, Publisher, 1940) This part is supplemented by a comprehensive section by J B Bateman on the physicochemical properties of large molecules (micellae, films, membranes) and their architectural and functional significance in living matter

The main subject of cellular physiology, by Hober, is contained in the subsequent six sections They deal with the architecture of protoplasm, the surface of the protoplast, its properties and architecture, and the influence of some extracellular factors on cellular activity and on passive penetration and active transfer in animal and plant tissues This part of the work includes a section on respiration of cells and tissues, by D R Goddard, and another on contractility, by W O Fenn The limitation of the final six sections to about 400 pages and the neglect of several recent physicochemical aspects of physiology were necessitated by war conditions, as Hober states in the preface Nevertheless, an incredible amount of information and valuable references will be found in these pages

There is scarcely a problem in ophthalmology whose study would not be benefited by the basic and broad information contained in Hober's book—whether on permeability, penetration and active transfer, respiration of tissues or the basic principles of physical chemistry Hober's hope that the text may be a "guide to new roads into the unknown" applies also to research in ophthalmology This book should be an integral part of the library in any biologic laboratory

LUDWIG VON SALLMANN

# Directory of Ophthalmologic Societies \*

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President Dr P Baillart, 66 Boulevard Saint-Michel, Paris, 6<sup>e</sup>, France  
Secretary-General Prof M Van Duyse, Université de Gand, Gand, Prov Ost-flandern, Belgium  
All correspondence should be addressed to the Secretariat, 66 Boulevard Saint-Michel, Paris, 6<sup>e</sup>, France

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Secretary Dr Ehlers, Jerbanenegade 41, Copenhagen, Denmark

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Place Habana, Cuba Time February 1948

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Secretary Dr C K Lin, 180 Hsi-Lo-yen Chienmeng, Peiping  
Place Peiping Union Medical College, Peiping Time Last Friday of each month

\* Secretaries of societies are requested to furnish the information necessary to make this list complete and keep it up to date

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 All correspondence should be addressed to the Assistant Secretary

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Place Good Samaritan Hospital, Portland Time Third Tuesday of each month

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Secretary Dr Benjamin F Souders, 143 N 6th St, Reading  
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 Secretary-Treasurer Dr Linley C Happ, 124 Waterman St, Providence  
 Place Rhode Island Medical Society, Library, Providence Time 8 30 p m  
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 Secretary-Treasurer Dr Louis Freimark, 256 Rochester Ave, Brooklyn 13  
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 from October to June The November, January and March meetings are  
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 Secretary Dr John H Barrett, 1304 Walker Ave, Houston, Texas  
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 Secretary Dr J Lawrence Sims, 305 Hume Mansur Bldg, Indianapolis  
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 Secretary Dr W E Keith, 1103 Grand Ave, Kansas City, Mo  
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 Secretary-Treasurer Dr Robert G Thornburgh, 117 E 8th St, Long Beach, Calif  
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 Secretary-Treasurer Dr K C Brandenburg, 110 Pine Ave, Long Beach 2, Calif  
 Place Los Angeles County Medical Association Bldg, 1925 Wilshire Blvd Time  
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 Secretary-Treasurer Dr J W Fish, 321 W Broadway, Louisville, Ky  
 Place Brown Hotel Time 6 30 p m, second Thursday of each month from September to May, inclusive

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 Secretary Dr James J Monohan, 31 S Jardin St, Shenandoah, Pa

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 Secretary Dr Frazier Williams, 1801 I St N W, Washington  
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 Secretary Dr Sam H Sanders, 1089 Madison Ave, Memphis, Tenn  
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 Secretary-Treasurer Dr Maitland D Place, 981 Reibold Bldg, Dayton, Ohio  
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President Dr J Rosenbaum, 1396 Ste Catherine St W, Montreal Canada  
 Secretary Dr L Tessier, 1230 St Joseph Blvd E, Montreal, Canada  
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Chairman Dr. M M Cullom, 700 Church St, Nashville, Tenn  
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 Place James Robertson Hotel Time 6 30 p m, third Monday of each month from October to May



## NEW ORLEANS OPHTHALMOLOGICAL AND OTOLARYNGOLOGICAL SOCIETY

President Dr W B Clark, 1012 American Bank Bldg, New Orleans  
 Secretary Dr Mercer G Lynch, 1018 Maison Blanche Bldg, New Orleans  
 Place Louisiana State University Medical Bldg Time 8 p m, second Tuesday  
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 Secretary Dr Milton Berliner, 57 W 57th St, New York  
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 Secretary Dr Benjamin Esterman, 983 Park Ave, New York 28  
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 Secretary Dr William Mussil, Medical Arts Bldg, Oklahoma City  
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 tember to May

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OTO-LARYNGOLOGICAL SOCIETY

President Dr A A Steinberg, 1502 Farnam St, Omaha  
 Secretary-Treasurer Dr W Howard Morrison, 1500 Medical Arts Bldg, Omaha 2  
 Place Omaha Club, 20th and Douglas Sts, Omaha Time 6 p m dinner, 7 p m  
 program, third Wednesday of each month from October to May

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 Secretary-Treasurer Dr J Averbach, 435 Clifton Ave, Clifton, N J  
 Place Paterson Eye and Ear Infirmary Time 9 p m, last Friday of every  
 month, except June, July and August

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 Secretary Dr Robert T M Donnelly, 255 S 17th St, Philadelphia  
 Time First Thursday of each month from October to May

## PITTSBURGH OPHTHALMOLOGICAL SOCIETY

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 Secretary Dr Robert J Billings, Park Bldg, Pittsburgh  
 Place Pittsburgh Academy of Medicine Bldg Time Fourth Monday of each  
 month, except June, July, August and September

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 Secretary Dr Paul C Craig, 232 N 5th St, Reading, Pa  
 Place Wyomissing Club Time 6 30 p m, third Wednesday of each month  
 from September to July

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 Secretary Dr Clifford A Folkes, Professional Bldg, Richmond, Va  
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 October to May

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President Dr Frank Barber, 75 S Fitzhugh St, Rochester, N Y  
 Secretary-Treasurer Dr Charles T Sullivan, 277 Alexander St, Rochester, N Y

ST LOUIS OPHTHALMIC SOCIETY

President Dr A Lange, 3903a Olive St, St Louis  
 Secretary Dr William Kleinberg, Frisco Bldg, St Louis  
 Place Oscar Johnson Institute Time Fourth Friday of each month from October  
 to April, inclusive, except December, at 8 00 p m

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 Secretary-Treasurer Lt Col John L Matthews, AAF School of Aviation Medicine,  
 Randolph Field, Texas  
 Place San Antonio, Brooke General Hospital, Randolph Field or San Antonio  
 Aviation Cadet Center Time 7 p m, second Tuesday of each month from  
 October to May

SAN FRANCISCO COUNTY MEDICAL SOCIETY, SECTION ON EYE,  
 EAR, NOSE AND THROAT

Chairman Dr C B Cowan, 490 Post St, San Francisco  
 Secretary Dr D Harrington, 384 Post St, San Francisco  
 Place Society's Bldg, 2180 Washington St, San Francisco Time Fourth  
 Tuesday of every month except June, July and December

SHREVEPORT EYE, EAR, NOSE AND THROAT SOCIETY

President Dr David C Swearingen, Slattery Bldg, Shreveport, La  
 Secretary-Treasurer Dr Kenneth Jones, Medical Arts Bldg, Shreveport, La  
 Place Shreveport Charity Hospital Time 7 30 p m, first Monday of every  
 month except July, August and September

SPOKANE ACADEMY OF OPHTHALMOLOGY AND OTO-LARYNGOLOGY

President Dr Clarence A Veasey Sr, 421 W Rivers de Ave, Spokane, Wash  
 Secretary Dr Clarence A Veasey, 421 W Riverside Ave, Spokane, Wash  
 Place Spokane Medical Library Time 8 p m fourth Tuesday of each month  
 except June, July and August

SYRACUSE EYE, EAR, NOSE AND THROAT SOCIETY

President Dr A H Rubenstein, 713 E Genesee St Syracuse, N Y  
 Secretary-Treasurer Dr I H Blaisdell, 713 E Genesee St, Syracuse, N Y  
 Place University Club Time First Tuesday of each month except June, July  
 and August

TOLEDO EYE, EAR, NOSE AND THROAT SOCIETY

Chairman Dr W W Randolph, 1838 Parkwood Ave, Toledo 2, Ohio  
 Secretary Dr John L Roberts, 316 Michigan St, Toledo, Ohio  
 Place Toledo Club Time Each month except June July and August

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Chairman Dr R G C Kelly, 14 Lynwood Ave, Toronto 5, Canada

Secretary Dr Alfred Elliott, 802 Medical Arts Bldg, Toronto 5, Canada

Place Academy of Medicine, 13 Queens Park Time First Monday of each month, November to April

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Secretary-Treasurer Dr Richard W Wilkinson, 1408 L St N W, Washington, D C

Place Medical Society of District of Columbia Bldg, 1718 M St N W, Washington, D C Time 7 30 p m, first Monday in November, January, March and May

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Chairman Each member in turn

Secretary Dr Samuel T Buckman, 70 S Franklin St, Wilkes-Barre, Pa

Place Office of chairman Time Last Tuesday of each month from October to May

## CHANGES IN LENS OF EMBRYO AFTER RUBELLA

Microscopic Examination of Eight Week Old Embryo

FREDERICK C CORDES, M D

AND

AELETA BARBER, M A

SAN FRANCISCO

SINCE the publication of Gregg's<sup>1</sup> paper on congenital cataract following rubella in the mother, the condition has been observed and reported a sufficient number of times to establish it as an entity. The histologic changes in the lens of an embryo after rubella have not been previously described in the literature.

Up to the present time a total of 170 cases of rubella during pregnancy have been reported, in 125 of which, or 73 per cent, congenital defects of the lens occurred in the child. In all these cases the mother contracted rubella during the first three months of pregnancy. In no instance in which an ocular defect occurred was the attack of rubella reported to have occurred after the third month.

Recently, a single eye of an 8 week old embryo has been received at the Ophthalmic Laboratory of the University of California and it is felt that a histologic study of this specimen may shed light on the question of the initial action of the causative agent of rubella on the lens.

### DESCRIPTION OF SPECIMEN

The specimen consisted of an embryonic eye recovered after a therapeutic curettage which ended a pregnancy of eight weeks. The clinical history reported that the patient was a 32 year old primipara. The fetus was in the left mentoposterior position on Feb 13, 1945, the diagnosis of rubella was made on March 23, and curettage was done on April 14. The specimen was prepared by the pyroxylin method, serial sections were cut at a thickness of 6 microns and stained with hematoxylin and eosin.

Microscopic examination revealed that the surface epithelium was absent (artifact) and the lids did not cover the eye.

The optic cup was well formed, and the outer layer was fully pigmented. The outer and inner walls of the optic cup had become approximated, and the fetal

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This study was made possible by funds from the E S Heller donations.

From the Ophthalmic Laboratory of the Division of Ophthalmology, University of California Medical School.

<sup>1</sup> Gregg, N M. Congenital Cataract Following German Measles in Mother. *Tr Ophth Soc Australia* 3:35-46, 1942.

fissure had closed. The hyaloid system was fully developed, and the hyaloid artery contained blood. The posterior portion of the retina had differentiated into two layers, the inner and outer neuroblastic layers, which were separated by the transient layer of Chievitz. Ganglion cells had migrated into the marginal zone, and their fibers had reached the optic stalk.

Mesodermal tissue covered the anterior surface of the lens, but the anterior chamber had not formed. The anterior portion of the tunica vasculosa lentis was poorly defined, but the lateral and posterior portions appeared normal.

The subcapsular epithelium of the lens showed distortion and disorientation

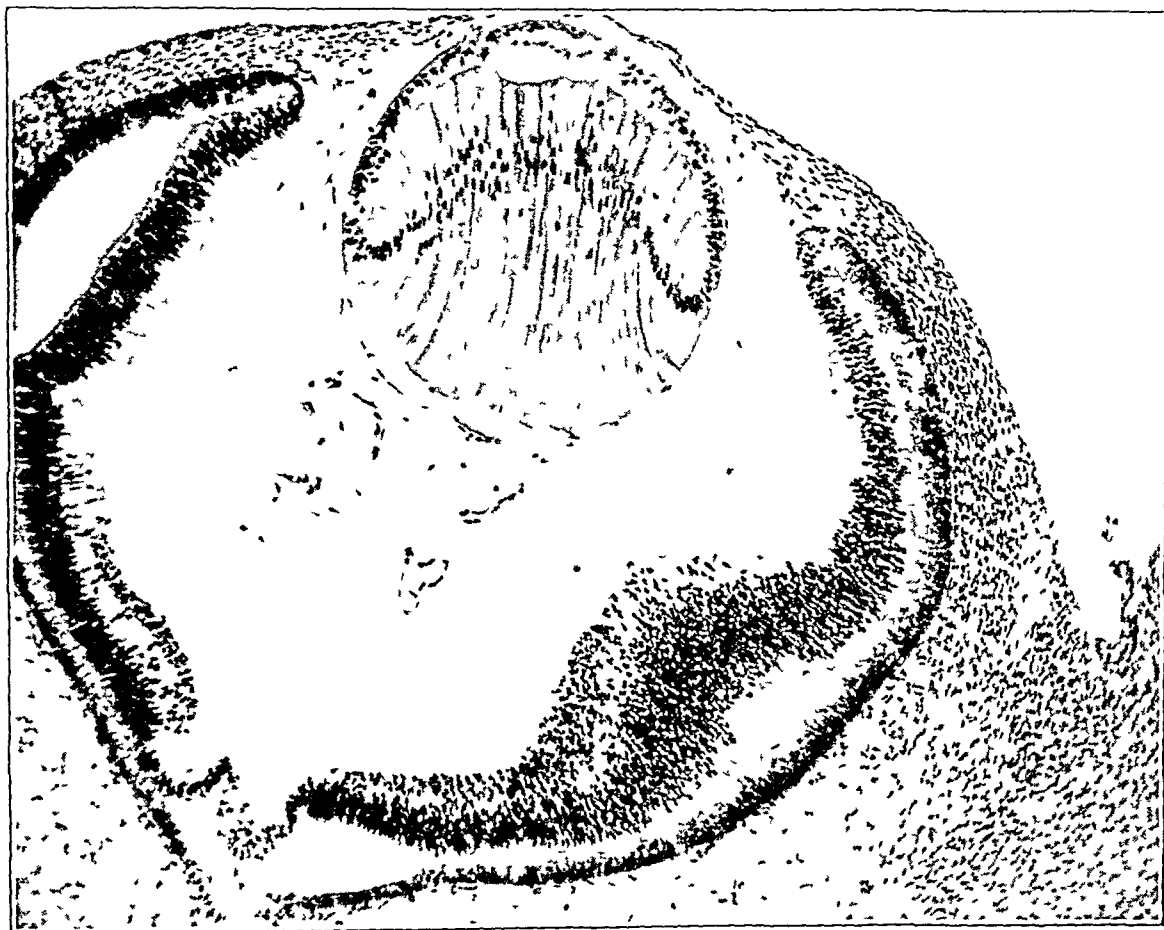


Fig 1—Fetal eye, showing development of the retina and the posterior portion normal for a fetus 19 mm in length and development of the lens and the anterior segment comparable to a fetus 17 mm in length, with retardation of the lens

of the cells at the anterior pole. The primary fibers had elongated but did not completely fill the cavity of the lens vesicle. These fibers were swollen and stained poorly, appearing vacuolated at their anterior ends. The nuclei also stained unevenly. The lens capsule was difficult to trace.

Since measurement of this embryo was impossible, the sections were compared with sections from normal embryos of 18 mm (6 weeks) and 24 mm (7 weeks), of which accurate measurements were obtained. The stage of development of

the posterior portion of this eye was approximately that of a 7 week old embryo, the lens showing retarded development, with vacuolation and early degeneration of the primary fibers at the anterior pole

Thus, the comparison revealed that the posterior portion of the eye, including the retina and the hyaloid system, were normally developed for an embryo of about 7 weeks, while, in the anterior portion, the lens and the anterior chamber were retarded

In the normal development of the eye the cavity of the lens vesicle is obliterated by the 16 mm stage, or the sixth week (Mann<sup>2</sup>) Serial sections of this



Fig 2—Anterior portion of the lens, showing failure of primary fibers to fill the cavity of the lens vesicle and vacuolation of primary fibers,  $\times 500$

specimen showed that a small remnant of this cavity still remained at the seventh to the eighth week This fact, together with the distortion and vacuolation of the anterior ends of the primary fibers, would indicate that the action of the toxic agent had occurred approximately during the sixth week of embryonic life This coincides with the clinical history of rubella during the sixth week of pregnancy

<sup>2</sup> Mann, I C Development of the Human Eye, London, Cambridge University Press, 1928, p 55

From the observations it is apparent that there were definite retardation and interference with the development of the lens

A section of the specimen was sent to Dr T L Terry, who reported as follows

"The section of the embryonic eyes in the case of maternal rubella appeared normal per se. The lens vesicle, which was not completely obliterated, contained amorphous, acidophilic material. Although this section was perhaps not at the proper level to show the greatest thickness of the vesicle, the anteroposterior diameter measured 350 microns. This lens vesicle corresponded in stage of differentiation and in size to that in the 17 mm stage, as verified both in the Minot Embryological Collection, at Harvard University, and in Mann's "Development of the Human Eye". The stage of retinal differentiation and the over-all size of the eyes, on the other hand, corresponded to the condition in the 19 mm stage. Needless to say, there is considerable difference in differentiation of the eye even in the 17 and the 19 mm stage.

From the comparative study, it is evident that the development of the crystalline lens in this specimen did not keep pace with the differentiation of the eye as a whole, a point of importance to be evaluated again when more such specimens are available

#### COMMENT

Swan<sup>3</sup> published a report of the pathologic changes in 3 infants who died of congenital defects due to rubella contracted by their mothers during the early stages of pregnancy. He found necrosis en masse of the nuclear portion of the lens. As he pointed out, whatever the pathologic process may be, it is evident that it had led to this necrosis en masse. He also found gross degenerative changes in and distortion and disorientation of the lens fibers formed subsequently from surviving cells in the equatorial region. This degeneration probably resulted from prolongation of action of the etiologic agent for some time after its initial attack on the lens. The distortion and disorientation could occur as the result of loss of normal tissue tension. That the effects of the pathologic process continue to be evident after the seventh to the eighth week was clear from the involvement of the secondary as well as primary fibers, since, as Mann<sup>2</sup> has pointed out, the secondary fibers are not formed until this period.

While the placenta acts as a barrier to the passage of bacteria, Needham<sup>4</sup> has pointed out that the ultrafiltrable viruses can pass through the placenta into the fetal circulation in man. From the work of Shuman,<sup>5</sup> Cohen and Scadron,<sup>6</sup> Canelli<sup>7</sup> and others, it is apparent

3 Swan, C. A Study of Three Infants Dying from Congenital Defects Following Maternal Rubella in the Early Stages of Pregnancy, *J Path & Bact* **56** 289-295 (July) 1944

4 Needham, J. *Chemical Embryology*, London, Cambridge University Press, 1931, vol 3, p 1503

5 Shuman, H H. Varicella in the Newborn, *Am J Dis Child* **38** 564-570 (Sept) 1939

that the placental permeability varies a good deal. During the last two months of pregnancy placental transmission does not occur, a fact which accounts for the less pronounced effect of infection at that time.

Reuss<sup>8</sup> expressed the opinion that intrauterine infection occurs through either the placenta or the amniotic fluid. The injury that the fetus suffers in cases of septic disease of the mother may be due primarily to toxic substances rather than to the transmission of bacteria from the maternal blood to the fetal circulation. The amniotic fluid may become infected by bacteria passing through the intact fetal membranes and therefore could easily become infected with a filtrable virus. Erickson<sup>9</sup> mentioned that embryonic tissues are particularly susceptible to virus infection.

It is conceivable that, in addition to transmission of the virus through the blood stream via the placenta, the embryo, especially the eyes, may also be affected through direct contact with the amniotic fluid. As Reese<sup>10</sup> has stated, the process which involves all but the outermost layers of the lens must have begun rather early in the life of the embryo. A review of the literature fails to reveal a single case of cataract formation in which the mother had rubella after the third month.

The foregoing observations offer the basis of a possible explanation for the limitation of changes in the lens to those cases in which rubella occurs during the first three months of pregnancy. It also seems to account for the rapid decline in the number of cases during the third month. According to Mann,<sup>11</sup> the anterior chamber appears about the 18 mm stage (sixth week), and the endothelium is well established by the 25 mm stage (7 weeks). Descemet's membrane is first recognized with certainty at the 76 mm stage (twelfth week)<sup>12</sup> and Bowman's membrane makes its appearance at the 103 mm stage (fifteenth week)<sup>13</sup>. The lids cover the eye at the 37 mm stage (ninth week)<sup>14</sup>. At the time

6 Cohen, P., and Scadron, S. J. The Placental Transmission of Protective Antibodies Against Whooping Cough, *J. A. M. A.* **121**:656-662 (Feb. 27) 1943.

7 Canelli, A. F. Sur le comportement normal et pathologique de l'immunité antimorbillieuse chez le nourrisson jeune, *Rev. franç. de pédiat.* **5**:668-680 (Dec.) 1929.

8 Reuss, A. R. Die Krankheiten des Neugeborenen, Berlin, Julius Springer, 1914, p. 533.

9 Erickson, C. A. Rubella Early in Pregnancy Causing Congenital Malformations of Eyes and Heart, *J. Pediat.* **25**:281-283 (Oct.) 1944.

10 Reese, A. B. Congenital Cataract and Other Anomalies Following German Measles in the Mother, *Am. J. Ophth.* **27**:483-487 (May) 1944.

11 Mann, J. p. 239.

12 Mann, J. p. 240.

13 Mann, J. p. 241.

14 Mann, J. p. 259.



at which the virus presumably acted on this specimen, the sixth week, the lids had not covered the eye, nor had Descemet's or Bowman's membrane been formed, so that rapid action of the toxic agent in the amniotic fluid on the anterior structures of the developing eye seems quite plausible. The protection afforded by the lids and by Descemet's and Bowman's membranes may form a sufficient barrier to protect the lens from initial damage after the third month and may explain the absence of changes in the lens due to rubella after the third month.

The study of more such specimens is necessary before any conclusions can be reached and before the changes described here can be said to be typical.

#### SUMMARY

Microscopic examination of the eye of a 7 to 8 week embryo with a history of rubella during the sixth week of pregnancy revealed definite changes in the lens.

The lens showed definite retardation of development and differentiation, while the posterior segment of the eye seemed normal.

The absence of the protection of the lids and of Descemet's and Bowman's membranes during the first three months of pregnancy may permit the toxic agent in the amniotic fluid to act fairly directly on the lens during this time.

The presence of these barriers after the third month may explain the absence of initial changes in the lens after that time.

The study of more specimens is necessary in order to evaluate the changes reported here.

## NIGHT VISION

### I A Comparison of the Scotopic Visual Ratings of Young Japanese and Caucasian Adults Living in Hawaii

WILLIAM JOHN HOLMES, M D

HONOLULU, TERRITORY OF HAWAII

FOR TWO years after the war began residents of the Territory of Hawaii lived under conditions of rigidly enforced nightly blackouts

The maintenance of vital public utilities, hospitals, docks, ship repair yards and scores of other essential activities, however, required that many employees continue their duties during the hours of blackout. It soon became evident that under conditions of absence of or greatly reduced artificial illumination some workers were less able to carry on their usual occupations than were others. The preponderance of those who were so handicapped were of Japanese ancestry.

In the capacity of chief of the Light Control Section of the Office of the Military Governor of the Territory of Hawaii and as a practicing ophthalmologist, I had numerous occasions to observe this "racial" trend of inferior scotopic seeing ability. In 1943 I reported this observation to the Headquarters of the Army Air Forces, as I felt that if racial inequalities in night vision really existed they might have far reaching tactical implications. Through the courtesy and cooperation of the Air Surgeon, Major General David N W Grant, several instruments were obtained from the War Department, and a Night Vision Laboratory was established in Honolulu.

The seeming urgency of time, the nonexistence of local technical library facilities, the lack of opportunity for scientific exchange of opinions, censorship regulations and other wartime restrictions, all impeded a comprehensive analysis and a full interpretation of the accumulated data.

This study is submitted merely as an additional, though incomplete, contribution to the constantly growing literature on night vision, presenting the subject from the standpoint of comparative physiology.

The object of this study was to investigate the respective visual abilities of two racial groups in regard to (1) photopic vision, expressed on the Snellen test chart, (2) scotopic vision, recorded on (a) the Hecht-Shlaer adaptometer,<sup>1</sup> (b) the S A M Night Vision Tester,<sup>2</sup>

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<sup>1</sup> Hecht, S, and Shlaer, S. An Adaptometer for Measuring Human Dark Adaptation. *J Optic Soc America* 28:269, 1936.

(Footnotes continued on next page)

(c) the Luckiesh-Moss Low Contrast Test Chart,<sup>3</sup> (d) the Bishop Harman Disc Spotting Device<sup>4</sup> and (e) the Ferree-Rand Projecto-chart<sup>5</sup> and (3) yellow and blue perception, estimated on the Ishihara color chart

#### PROCEDURE

The subjects tested were unselected junior and senior high school students of both sexes, ranging from 17 to 19 years of age. The tests were conducted, by the same examiner, in two of Honolulu's public high schools noted for the preponderance of their Caucasian and Japanese enrolments, respectively. The cooperation of the students was secured by telling them the results of their individual examinations on completion of the tests. Dark adaptation was achieved by a preliminary waiting period of thirty minutes in a completely darkened room. During this time the students were told that they would be shown various figures and forms at low intensities of illumination. They were advised to view these forms out of the corners of their eyes rather than by looking at them directly.

The actual tests were carried out binocularly, as follows

1 Measurements were taken of the thresholds of light and forms on the Hecht-Schlaer adaptometer

2 Determinations were made on the S A M Night Vision Tester of the subject's abilities to recognize the position of the break in a 2 degree Landolt C on the darkest, but still barely visible, background. The light source of this instrument consisted of a plaque of self-luminous paint, the brightness of which was reduced with a series of neutral filters. The illuminated field subtended a visual angle of approximately 35 degrees. The tests were carried out at a distance of 14 inches (35.5 cm) from the eyes. Four out of five correct answers were required before a final score was given. The brightnesses of the illuminated area with the various filters in position are shown in the following tabulation

| Filter | Brightness of Background,<br>Log Micromicrolamberts |
|--------|---|
| 1      | 4.8   |
| 2      | 4.6   |
| 3      | 4.5   |
| 4      | 4.3   |
| 5      | 4.2   |
| 6      | 4.0   |
| 7      | 3.9   |
| 8      | 3.7   |
| 9      | 3.6   |
| 10     | 3.4   |

3 Quantitative measurements of contrast vision were recorded on a slightly modified form of Harman's Disc Spotting Device. In this test the subjects were asked to identify the correct number of white round disks, which were arranged

2 Rowland, W. M., and Campbell, P. A. A Small Light Threshold Meter, A. A. F. School of Aviation Medicine, Research Report no. 2, Project no. 69, Randolph Field, Texas, Jan. 23, 1943.

3 Luckiesh, M., and Moss, F. K. The Ability to See Low Contrasts at Night, *J. Aeronaut. Sci.* **9** 1, 1942.

4 Harman, N. B. Testing Night Vision, *Brit. M. J.* **1** 636, 1941.

5 Ferree, C. E., and Rand, G. Visual Acuity at Low Illuminations Apparatus and Results, *Tr. Am. Ophth. Soc.* **17** 370, 1919.

in four corners of a black velvet square. The disks measured  $\frac{1}{2}$  inch (1.3 cm) in diameter and were placed  $\frac{1}{8}$  inch (0.3 cm) apart.

4 Qualitative measurements of contrast vision were estimated on the Luckiesh-Moss Low Contrast Test Chart. This was done by asking the subjects to decipher dark digits on a white background, photometrically reduced to present successively less contrast with each other. According to Luckiesh and Moss, the per cent contrasts represented by the various lines on their chart were as follows

| Line No | Per Cent Contrasts |
|---------|--------------------|
| 20      | 39.7               |
| 19      | 37.8               |
| 18      | 35.9               |
| 17      | 34.0               |
| 16      | 32.1               |
| 15      | 30.2               |
| 14      | 28.3               |
| 13      | 26.4               |
| 12      | 24.5               |
| 10      | 20.7               |
| 8       | 16.9               |
| 6       | 13.1               |
| 4       | 9.4                |
| 2       | 5.6                |
| 1       | 3.8                |

Brightness contrast, in this test, is defined as the difference between the brightnesses (or reflection factors) of background and object, divided by the brightness (or reflection factor) of the background. The reflection factor of the background has been calculated as approximately 80 per cent.

The charts used for both the Harman and the Luckiesh-Moss tests were illuminated with a standard 6 watt, incandescent white light bulb, mounted in a 12 by 12 inch (30 by 30 cm) black box. The box was placed at a distance of 10 feet (3 meters) from the charts and emitted bundles of light rays through a circular,  $\frac{1}{2}$  inch (1.3 cm) aperture. The voltage, from the main electric line, was reduced by means of a simple rheostat built within the box.

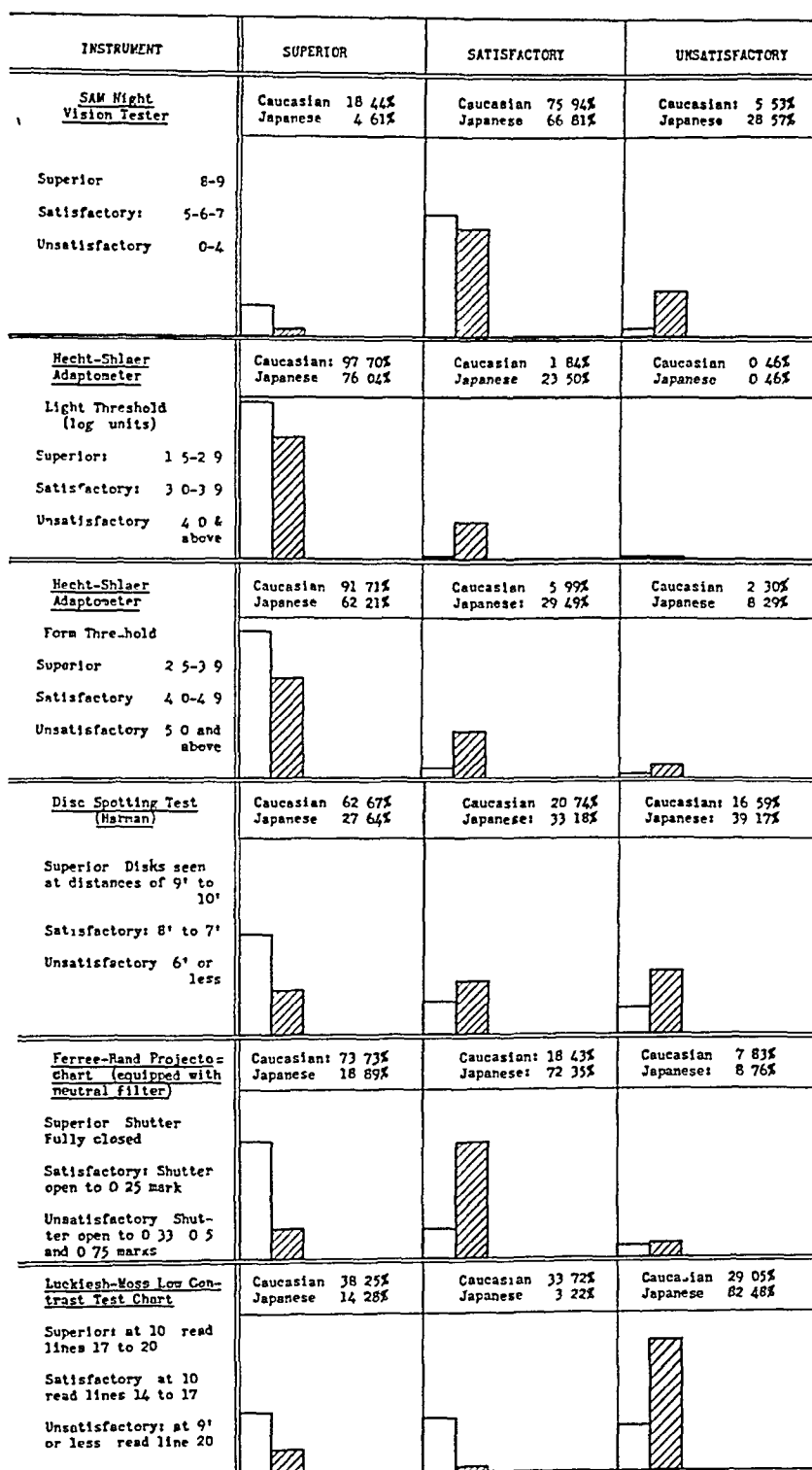
If a subject was not able to see the chart used in either of these two tests, he was asked to approach it slowly. The distance at which he was first able to identify the test objects correctly was taken as the numerator, and the line read on the Luckiesh-Moss chart, or the distances, in meters, at which the four groups of circles were correctly counted on the Harman chart, was taken as the denominator.

5 The minimum amount of light required for the recognition of the letters on the 10/200 line of the Ferree-Rand Projectochart was next ascertained. In this test, the light source was dimmed by placing a standard neutral filter in front of it and by closing the shutter of the instrument to the maximum. If a subject was unable to see the letters under these conditions, the shutter was gradually opened to the arbitrarily chosen positions of 0.25, 0.33, 0.50 and 0.75, until sufficient visibility was provided to enable him to recognize the letter E appearing in various positions on the screen.

6 and 7 Monocular tests of visual acuity on the Snellen chart and an evaluation of yellow and blue perception on the Ishihara color plates, using daylight illumination, concluded the examinations.

No measurements were made of the brightness levels at which tests 3, 4 and 5 were conducted. The only available brightness meter<sup>6</sup> in the Territory of Hawaii

<sup>6</sup> Model L-H, made by General Electric Company.



Graphic representation of the comparative night vision abilities of 217 Caucasian and 217 Japanese subjects

at the time these investigations were in progress was not sufficiently sensitive to register the amount of light reflected from the charts. Similarly, no readings were taken of the intensities of the light sources themselves, as the most sensi-

TABLE 1—Comparison of 217 Caucasian and 217 Japanese Subjects Regarding the Incidence of Myopia, Blue and Yellow Blindness and Photopic and Scotopic Vision

|   | Japanese Subjects Tested |            | Caucasian Subjects Tested |            |
|---|--------------------------|------------|---------------------------|------------|
|   | Number                   | Percentage | Number                    | Percentage |
|   | 217                      | 100        | 217                       | 100        |
| Glasses worn  | 84                       | 38.71      | 49                        | 22.58      |
| Myopia or myopic astigmatism  | 61                       | 28.11      | 11                        | 5.07       |
| Blue and yellow perception (Ishihara plates)                                      |                          |            |                           |            |
| Normal  | 213                      | 98.16      | 209                       | 96.31      |
| Absent  | 4                        | 1.84       | 8                         | 3.69       |
| Central, photopic vision taken with glasses, if such were worn (Snellen's rating) |                          |            |                           |            |
| Right 20/20 to 20/40  | 211                      | 97.23      | 209                       | 96.31      |
| Right less than 20/40   | 6                        | 2.79       | 8                         | 3.69       |
| Left 20/20 to 20/40   | 214                      | 98.62      | 211                       | 97.23      |
| Left less than 20/40  | 3                        | 1.38       | 6                         | 2.77       |
| S A M Night Vision Tester   |                          |            |                           |            |
| Lightest filter 0 to 4  | 62                       | 28.57      | 12                        | 5.53       |
| 5   | 58                       | 26.73      | 31                        | 14.29      |
| 6   | 60                       | 27.64      | 61                        | 28.11      |
| 7   | 27                       | 12.44      | 73                        | 33.64      |
| 8   | 9                        | 4.15       | 32                        | 14.75      |
| Darkest filter 9  | 1                        | 0.46       | 8                         | 3.69       |
| Hecht-Shlaer adaptometer  |                          |            |                           |            |
| Light threshold (log units)   |                          |            |                           |            |
| 15 to 29  | 165                      | 76.04      | 212                       | 97.70      |
| 30 to 39  | 51                       | 23.50      | 4                         | 1.84       |
| 40 and above  | 1                        | 0.46       | 1                         | 0.46       |
| Form threshold (log units)  |                          |            |                           |            |
| 25 to 39  | 135                      | 62.21      | 199                       | 91.71      |
| 40 to 49  | 64                       | 29.49      | 13                        | 5.99       |
| 50 and above  | 18                       | 8.29       | 5                         | 2.30       |
| Harman Disk Spotting Test   |                          |            |                           |            |
| At distances of 10' to 9'   | 60                       | 27.64      | 136                       | 62.67      |
| 8' to 7'  | 72                       | 33.18      | 45                        | 20.74      |
| 6' to 5'  | 75                       | 34.56      | 24                        | 11.06      |
| 4' or less  | 10                       | 4.61       | 12                        | 5.53       |
| Ferree Rand Projectochart equipped with neutral filter                            |                          |            |                           |            |
| With shutter fully closed   | 41                       | 18.89      | 160                       | 73.73      |
| With shutter open to 0.25 mark  | 157                      | 72.35      | 40                        | 18.43      |
| With shutter open to 0.33 mark  | 12                       | 5.53       | 14                        | 6.45       |
| With shutter open to 0.5 mark   | 7                        | 3.23       | 3                         | 1.38       |
| With shutter open to 0.75 mark  |                          |            |                           |            |
| Luckesh Moss Low Contrast Test Chart  |                          |            |                           |            |
| At 10' read lines 20 and 19   | 17                       | 7.83       | 35                        | 16.13      |
| At 10' read lines 18 and 17   | 14                       | 6.45       | 48                        | 22.12      |
| At 10' read lines 16 and 15   | 3                        | 1.38       | 31                        | 14.29      |
| At 10' read lines 14 or less  | 4                        | 1.84       | 40                        | 18.43      |
| At 9' read lines 20   | 37                       | 17.05      | 19                        | 8.76       |
| At 8' read lines 20   | 46                       | 21.20      | 18                        | 8.30       |
| At 7' read lines 20   | 38                       | 17.51      | 8                         | 3.69       |
| At 6' read lines 20   | 29                       | 13.36      | 9                         | 4.15       |
| At 5' read lines 20   | 29                       | 13.36      | 9                         | 4.15       |

tive available light meter,<sup>7</sup> even at a distance of 1 foot (30 cm) from the light source, failed to produce any perceptible excursion of the indicator needles. Slight, hour to hour or day to day variations in the current supplying the light

7 Model 164, manufactured by Weston Electrical Instrument Corporation

sources in these tests were also left with no accounting. However, the real point at issue was a comparative study of racial differences in scotopic visibility under identical conditions of low intensity illumination, for this reason, even though a knowledge of the exact brightness measurements at which the tests were carried out would have been desirable, it was not considered essential.

#### HEREDITARY FACTORS

The theory of racial differences in sensory acuity has been promulgated in the literature from time to time. When such differences in ocular function are found, their scientific interpretation must take into account variations in the configuration of the human eye and its adnexa, differences in the dietary customs and habits of daily life and pathologic conditions affecting the eyes themselves.

In 1905 Wolflin<sup>8</sup> reported that dark-haired persons had faster adaptation and lower thresholds than blondes. In 1933 Helson and Guilford<sup>9</sup> stated that Negroes attained much lower thresholds than white persons. These observations were contradicted by Matthey,<sup>10</sup> who found no differences in the dark adaptation curves between subjects with light eyes and those with heavily pigmented eyes.

#### MORPHOLOGIC FACTORS

The average dimensions of the bony orbits of Caucasian and of Japanese subjects are cited from Martin<sup>11</sup> and Adachi,<sup>12</sup> as follows:

Orbital Height Measured vertically across the orbital hiatus, from the lower to the upper margin, at right angles to the breadth of the axis

| Japanese | Caucasian |
|----------|-----------|
| 33       | 34        |

Orbital Breadth Measured transversely across the orbital hiatus, from medial to lateral margin (mm)

| Japanese | Caucasian |
|----------|-----------|
| 38       | 36        |

Orbital Depth Measured anteroposteriorly from the rim to the apex of the superior, inferior, medial and lateral walls (mm)

|          | Japanese | Caucasian |
|----------|----------|-----------|
| Medial   | 41.7     | 43.8      |
| Lateral  | 48.3     | 43.9      |
| Superior | 51.8     | 48.6      |
| Inferior | 49.2     | 46.4      |

Inclination of the breadth of the axis of the orbit (Inches)

|        | Japanese | Caucasian |
|--------|----------|-----------|
| Male   | 13.8     | 16.2      |
| Female | 11.9     | 13.9      |

Breadth of palpebral fissure (mm)

| Japanese | Caucasian |
|----------|-----------|
| 28.9     | 31.0      |

8 Wolflin, E. Der Einfluss des Lebensalters auf den Lichtsinn bei Dunkeladaptiertem, *Arch f Ophth* **61** 524, 1905

9 Helson, H., and Guilford, J. P. The Relation of Visual Sensitivity to the Amount of Retinal Pigmentation, *J Gen Psychol* **9** 58, 1933

10 Matthey, G. Eine Standardkurve der Dunkeladaptation für klinische Untersuchungen, *Arch f Ophth* **61** 524, 1905

11 Martin, R. *Lehrbuch der Anthropologie*, Jena, Gustav Fischer, 1928, vols 1 and 2

12 Adachi, B. Die Orbita und die Hauptmasse des Schädels der Japaner, *Ztschr f Morphol u Anthropol* **7** 379, 1904

## MYOPIA

Errors of refraction were noted in 84 subjects of the Japanese group and in 49 subjects of the Caucasian group. Of the 84 Japanese subjects who wore glasses, 61 had myopia or myopic astigmatism. Of the 49 Caucasian subjects wearing glasses, only 11 with myopia or myopic astigmatism were found. No refractions or examinations of the fundus were made on any of the students during the course of these investigations. Hence, an appraisal of their refractive status was based entirely on neutralization of the glasses which they were wearing.

The foregoing observations indicate a greater frequency of myopia among Oriental than among Caucasian subjects. This observation is supported by Rasmussen,<sup>13</sup> who reported an incidence of 53 per cent of myopia among Chinese students attending various mission schools throughout China. Whether a congenital predisposition toward the development of myopia actually exists among Orientals or whether the condition represents the end results of debility of nursing mothers, vitamin deficiency in infant foods or the excessive use of the eyes for near work under poor lighting conditions is not known. Jackson<sup>14</sup> pointed out that myopia often occurs in eyes that have been damaged from childhood by corneal inflammation or trauma, even though only one eye may have been affected. Thus, trachoma, with its sequelae, may well be a contributory cause in the development of myopia among those Oriental subjects who have been afflicted with the disease in their youth. According to Walker<sup>15</sup> and Law,<sup>16</sup> calcium and parathyroid deficiencies also play a part in the causation of myopia. Generally speaking, myopia predominates in dolicocephalic persons and is found in persons with a slender type of body build, these characteristics are more common in the Japanese than in the Caucasian race.

Rutherford<sup>17</sup> stated that myopia in a given patient is the end result of a number of conditions working together and that the etiologic factors are not the same in all cases.

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13 Rasmussen, O. D. Incidence of Myopia in China. Data and Theses from Periodical Investigations Covering Thirty Years' Residence and Association with Refracting and Hospital Centers in a Score of the Larger Cities, *Brit J Ophth* **20**:350, 1936.

14 Jackson, E. Control of Myopia, *Am J Ophth* **14**:719, 1931.

15 Walker, J. P. S. Progressive Myopia. A Suggestion Explaining Its Causation and Treatment, *Brit J Ophth* **16** 483, 1932.

16 Law, F. W. Calcium and Parathyroid Therapy in Progressive Myopia, *Tr Ophth Soc U Kingdom* **54** 281, 1934.

17 Rutherford, C. W. Myopia. Etiology and Treatment, Graduate Lecture delivered before the American Academy of Ophthalmology and Otolaryngology, 1939.



Irrespective of the causes of myopia, it is generally agreed that thresholds for the recognition of objects at faint brightnesses are higher for myopic than for emmetropic and hyperopic eyes. It has been postulated that stretching of the inner layers of the retina of the near-sighted eyeball is responsible for a deficiency in the normal functioning of the retinal rods.

#### TRACHOMA

The subjects investigated in this study were not examined with the slit lamp. However, routine examination with the slit lamp of thousands of patients in Hawaii over a period of many years revealed a surprisingly large incidence of incipient pannus formation among persons of Oriental ancestry. The blood vessels, which invaded the corneas in these patients, often extended as much as 2 mm or more into the corneal stroma at the upper limbus. With a few exceptions, the condition was not associated with other clinical evidences of trachoma. Pannus formation was noted with such frequency among the Japanese residents of Hawaii that it was felt that the disease, in an attenuated form, is endemic among them. The early appearance of pannus in the course of trachoma has previously been emphasized by Wilson,<sup>18</sup> von Horváth<sup>19</sup> and others. MacCallan,<sup>20</sup> in 1938, reported an incidence of trachoma of 12 per cent among more than 1,000,000 recruits in Japan. He stated, however, that the disease was chiefly of a light type. From the files of the Bureau of Communicable Diseases of the Territory of Hawaii for an eight year period, extending from 1937 to 1944, Enright<sup>21</sup> found 331 cases of active trachoma. Of these, 183 (54.7 per cent) occurred among the Japanese and only 14 (4.2 per cent) among Caucasian subjects. In 1940 Hamman and I<sup>22</sup> reported that trachoma ranked third among the causes of blindness in Hawaii and that the disease took its heaviest toll from members of the Oriental population.

The relationship between deficiencies of scotopic function and the aftermaths of a previous attack of trachoma is largely a matter of conjecture. However, it does not seem too far fetched to assume that eyes which at one time have been the seat of an inflammation which

18 Wilson, R. P. A Short Slit-Lamp Study on the Corneal Vessels in Egyptian Trachoma, *Folia ophth orient* **1** 52, 1932.

19 von Horváth, B. Hornhaut bei Trachom, *Klin Monatsbl f Augenh.* **72** 242, 1924.

20 MacCallan, A. F. The World-Wide Distribution of Trachoma, *Brit J Ophth* **22** 513, 1938.

21 Enright, J. Personal communication to the author.

22 Holmes, W. J., and Hamman, G. C. Causes of Blindness in Hawaii, *Arch Ophth* **25** 643 (April) 1941.

resulted in corneal vascularization may, as a consequence, have suffered some disturbance in their metabolism, bringing about a decrease in their functional integrity.

#### NUTRITIONAL FACTORS

The importance of the nutritional state of the subject in relation to his ability to see in the dark cannot be sufficiently emphasized. In the present study it was both impractical and unfeasible to inquire into the dietary habits of each subject and to calculate his daily calory and vitamin intake. Fortunately, thorough and painstaking comparative studies, covering many years of observation of the dietary values of the various racial groups living in Hawaii, have been made by Miller<sup>23</sup> and her associates. Their researches indicate that with slight modifications the Japanese, along with most of the other racial groups, retained their own particular food habits in successive generations. In a study of the dietary and value of living of 44 Japanese families (252 persons)<sup>24</sup>

TABLE 2—*Percentage Distribution of the Total Calories in the Diet Among the Various Food Groups (Potgieter)*

|  | Cereals | Vegetables<br>and Fruits | Milk, Milk<br>Products | Meat, Fish,<br>Fats<br>and Eggs | Sweets |
|--|---------|--------------------------|------------------------|---------------------------------|--------|
| Japanese in Hawaii   | 59      | 13                       | 4                      | 11                              | 14     |
| Japanese in Japan  | 74      | 9.9                      | 0.4                    | 12                              | 7      |
| Stiebeling's * allowances for moderately<br>active male 20-60 years of age | 24      | 18                       | 19                     | 12                              | 27     |

\* Stiebeling, H. K., and Ward, M. M. *Diets at Four Levels of Nutritive Content and Cost*, Circular 296, United States Department of Agriculture, 1933, p. 53.

in Hawaii, Miller<sup>25</sup> called attention to deficiencies in the intakes of calcium and vitamins A and B in the diet. Potgieter,<sup>26</sup> from a similar study, calculated the nutritive elements of an average Japanese diet in Hawaii. Her figures are cited in tables 2 and 3 side by side with statistics showing the average components of an American diet and a Japanese diet consumed in Japan.

Inspection of the data given in table 3 shows a relatively low calcium and a relatively high phosphorus intake among the Japanese in Hawaii, producing a ratio of 1 part of calcium to 3 or 4 parts of phosphorus.

23 Miller, C. D., and Masunaga, E. *A Study of the Diet of Japanese Sampan Fishermen While at Sea*, Proc. Hawaiian Acad. Sc., Special Publication no. 30 of the Bernice P. Bishop Museum, 1935-1936, p. 8.

24 It is realized that the number of families studied in this group is small. However, it is felt, from similar studies, that the data are sufficiently reliable and representative to warrant analysis and discussion.

25 Miller, C. D. *A Study of the Dietary and Value of Living of Forty-Four Japanese Families in Hawaii*, Univ. Hawaii Bull. 18:2 (Dec.) 1938.

26 Potgieter, M. *Diet and Health in Rural Hawaii*, unpublished report.

It is believed that this ratio is inadequate for the normal maintenance of body metabolism. This belief is substantiated by the high clinical incidence of dental caries and rickets among the Japanese school children living in Hawaii. Sherman's<sup>27</sup> standards, which have been adopted by the Bureau of Home Economics, give a ratio of 1 part of calcium to less than 2 parts of phosphorus per adult male unit per day.

In a recent report, Knapp<sup>28</sup> emphasized the importance of a normal relationship of calcium and phosphorus in the diet with regard to night blindness. Of 93 patients with various degrees of myopia, he found 64 who complained of poor vision under conditions of reduced illumination. Forty-eight of the 64 patients noticed a distinct improvement with respect to their night blindness after several weeks of intensive therapy with vitamin D and calcium. Thus it would appear that the abnormal ratio of calcium and phosphorus in the Japanese diet might in some way alter the biochemical processes that regulate function of the rods and result in reduced scotopic visual efficiency.

TABLE 3—Average Daily Dietary Essentials for an Adult Male (Potgieter)

|                          | Calories | Protein<br>Gm | Calcium<br>Gm | Phosphorus<br>Gm | Iron<br>Gm | Vitamins |          |          |
|--------------------------|----------|---------------|---------------|------------------|------------|----------|----------|----------|
|                          |          |               |               |                  |            | A<br>I U | B<br>I U | C<br>I U |
| Japanese in Hawaii       | 3,240    | 82            | 0.37          | 1.35             | 19         | 3,960    | 270      | 2,340    |
| Stiebeling's* allowances | 3,000    | 67            | 0.68          | 1.35             | 15         | 6,000    | 500      | 1,500    |

\* Stiebeling, H. K., and Ward, M. M. Circular 296, United States Department of Agriculture, 1933, p. 58.

Further examination of table 3 reveals inadequate quantities of vitamins A and B in the average Japanese diet. The deficiency of vitamin A is partly accounted for by their low consumption of dairy products and green and yellow vegetables. In the absence of these sources, the main supply of vitamin A in the Japanese diet is derived from seaweeds and, to a lesser extent, from fish oils. Iseki<sup>29</sup> analyzed twelve commercial samples of edible Japanese seaweed and found that vitamin A was present in considerable quantities in all of them, while thiamine (vitamin B<sub>1</sub>) and riboflavin were detected in lesser amounts.

27 Sherman, H. C. *Chemistry of Food and Nutrition*, ed. 5, New York, The Macmillan Company, 1937, p. 532.

28 Knapp, A. A. Night Blindness, Improvement with Vitamin D, Including Experimental Production of Retinitis Pigmentosa and Its Treatment in Humans with Vitamin D, U. S. Nav. M. Bull. 41 373, 1943.

29 Iseki, K. An Investigation of Twelve Commercial Samples of Kobu-Edible Japanese Seaweed for Iodine Content and Vitamins, Thesis, University of Hawaii, 1942.

Jameson, Drummond and Coward<sup>30</sup> stated that certain marine diatoms grown in sterilized sea water to which nutrient solutions were added were capable of synthesizing large quantities of vitamin A. They concluded that the available supply of vitamin A in fish liver oils originated from various forms of marine algae. It must, however, be kept in mind that seaweeds as well as fish liver oils, are considered more or less a delicacy in Japan,<sup>31</sup> and often their high cost and the problems of transportation to inland communities preclude their extensive use.

In commenting on the importance of dairy products as sources of supply for vitamin A in the diet, the *Lancet*<sup>32</sup> recently reviewed studies made by Nylund, in Finland. Nylund examined a group of students in 1938 and another in 1940. Between these two dates dairy products had been rationed. Of the 1938 group, 79 per cent showed normal dark adaptation curves, 9 per cent were night blind and 12 per cent had borderline vision. Of the 1940 group, only 48 per cent had normal dark adaptation, 29 per cent were night blind and 23 per cent had borderline vision.

Vitamin B deficiencies among the Japanese group were primarily ascribed to the widespread use of highly milled cereal products, such as white rice, eggless noodles and white bread. Kondo<sup>33</sup> attributed the great frequency with which gastrointestinal disorders are met in Japan to the low intake of vitamin B by the mass of the people. Sugimoto,<sup>34</sup> in a recent report, urged the adoption of partly, instead of highly, milled rice as a means of improving the health of the people of Japan.

Laboratory evidence of the relative inadequacies of an average Japanese diet, as compared with an average American diet comes from an as yet unpublished experiment of Miller<sup>35</sup>. She found that rats weaned on a typical Japanese diet had fewer offspring, a shorter life span, higher mortality, slower growth and greater reduction in weight than a control group fed a typical American diet.

Space here does not permit a review of the special role played by vitamins A and B in the physiology of night vision. Suffice it to state

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30 Jameson, H. L., Drummond, J. C., and Coward, K. H. Synthesis of Vitamin A by a Marine Diatom Growing in Pure Culture, *Biochem J* **16** 482, 1922.

31 Kofume, K. Nutritional Condition of Farmers in Japan, *Ryoshoku Kenkyu*, 1937, no 129, p 19. Hara, T. School Lunches and Nutritional Menus, 205-207, 1936. Morimoto, K. The Efficiency Standard of Living in Japan, Japanese Council of the Institute of Pacific Relations, 1931.

32 Night Blindness, editorial, *Lancet* **2** 807, 1941.

33 Kondo, K. The Health and Foods of the People, *Ryoshoku Kenkyu*, 1936, no 142, p 2.

34 Sugimoto, K. Food Problems of the Crisis, *Ryoshoku Kenkyu*, 1938, no 143, p 32.

35 Miller, C. D. Personal communication to the author.

that Wald<sup>36</sup> demonstrated that vitamin A enters into the constitution of visual purple Hecht<sup>37</sup> showed that both the cone and the rod thresholds were raised by deprivation of vitamin A, rod vision, however, was affected more than cone vision Heiman<sup>38</sup> called attention to the presence of large amounts of riboflavin in the retina He found that a reduction of riboflavin in the diet produced dimness in vision, especially under conditions of reduced illumination He expressed the belief that riboflavin and carotene have similar characteristics and may be engaged in analogous functional processes

#### PSYCHOLOGIC FACTORS

In addition to the physiologic mechanisms involved, the ultimate appraisal of a subject's visual measurements must take into account his motivational patterns This is particularly true in night vision testing, in which, as stated in a previous paper,<sup>39</sup> the results of successive examinations are often inconsistent and may be influenced by scores of extrinsic and intrinsic factors affecting the individual or his environs

To illustrate During the course of these examinations, an 18 year old Japanese youth fainted, without any obvious cause When revived, he admitted that he had always been afraid of the dark and felt ill at ease when confined to dim, unilluminated quarters As a further illustration, a few typical comments, quoted verbatim from the high school paper<sup>40</sup> of one of the schools where the testing was done, are appended "Boy, did I feel lost!" exclaimed George S "It was so dark, I couldn't even see the nurse She certainly was pretty," he added, winking To make up for the darkness and monotony of waiting, Frances S and her chums indulged in boisterous singing "The whole affair meant a lot to me, because I know now that my chances for getting accepted as an aviation cadet are that much better," declared Bill T Said Georgia S "It would have been more fun if there had been some boys with us" Said Ruth C "I sat there and squirmed during the thirty minutes our eyes were becoming accustomed to the darkness Horrible things, like murders and mysterious disappearances, kept running through my mind"

These comments are cited only to show how a subject's responses may vary, depending on his attention, enthusiasm, fears and worries, at the time of the examination

36 Wald, G Carotenoids of the Visual Cycle, *J Gen Physiol* **19** 351, 1935

37 Hecht, S Rods, Cones and the Chemical Basis of Vision, *Physiol Rev* **17** 239, 1937

38 Heiman, M Riboflavin, *Arch Ophth* **28** 493 (Sept) 1942

39 Holmes, W J Night Vision, *Arch Ophth* **30** 267 (Aug) 1943

40 Blindness Test Pretty Nurse Attracts Students, *The Rough Rider* (Roosevelt) High School, Honolulu, T H ) **14** 29, 1944

## SUMMARY AND CONCLUSIONS

Two hundred and seventeen teen-aged high school students of Japanese ancestry and an equal number of students of Caucasian ancestry were subjected to identical tests of their day vision, night vision and yellow and blue perception

The day vision of the two groups tested on the Snellen chart showed no perceptible differences. It is noteworthy in this regard that less than 4 per cent of the subjects in each group had visual acuity of less than 20/40 which was not corrected with lenses

Glasses were worn by 38.7 per cent of the Japanese and by 22.58 per cent of the Caucasian group. Myopia or myopic astigmatism predominated in the Japanese group, being found in 28.11 per cent of the total number while it was noted in only 5.07 per cent of the total Caucasian group

Blue and yellow perception was essentially normal in each group. Only 1.84 per cent of the Japanese and 3.69 per cent of the Caucasian group failed on the test for this function

The Japanese group as a whole did more poorly on every one of the tests for night vision than did the Caucasian group

With the S A M Night Vision Tester, 28.57 per cent of the Japanese group frankly failed, 26.75 per cent barely passed and less than 5 per cent had superior ratings. Of the Caucasian group, in the same test, only 5.53 per cent failed, 14.29 per cent barely passed and 18 per cent had superior ratings

With the Hecht-Shlaer adaptometer, 24 per cent of the Japanese group required 3.0 or more log units of illumination for their light thresholds and only 2.3 per cent of the Caucasian group fell into this category. On the same instrument measuring form threshold visibility, 38 per cent of the Japanese group required 4.0 or more log units of illumination, among the Caucasian group only 8.3 per cent needed similar intensities in this test

The discrepancies found between the two races were especially conspicuous in the Harman, Ferree-Rand and Luckiesh-Moss tests. It is worthy of note that all three of these tests call for a more or less accurate differentiation of the test objects, requiring some degree of cone vision. It is theoretically possible that in these tests the retinal areas which were under investigation corresponded with, or were situated close to those which normally function at twilight, dusk and dawn and contain both rods and cones. The Japanese as a group hesitated, asked for more light or walked closer to the test charts before they would risk an answer

No relation was noted between high acuities or photopic and scotopic vision. Subjects with excellent distant vision at high intensities of

illumination often failed on all the tests conducted at low levels of illumination. The reverse, however, did not hold true. Subjects with poor distant vision, especially those with myopic errors of refraction, even though they wore correcting lenses, in most instances were below par in their night visual efficiency.

No direct relationship was found between yellow and blue blindness and night blindness. The lack of any correlation between these two functions is contrary to the observation of Riddell,<sup>41</sup> who reported that night-blind subjects were often unable to name the yellow and blue plates in Schilling's color book.

The working hypothesis adopted to account for the differences in scotopic visual ability between the two groups was based on the following considerations: (a) hereditary factors, embryologic (?) and morphologic (?) differences between the two races, (b) greater frequency of myopia among the Japanese, (c) greater frequency of trachoma among the Japanese, (d) inadequate dietary intakes of vitamins A and B in the Japanese diet, (e) inadequate amounts of calcium in the Japanese diet, (f) abnormal ratio of calcium and phosphorus in the Japanese diet. The vertical reading habit of the Japanese people has also been suggested as an additional factor responsible for their defective night vision. There is, however, no scientific evidence to substantiate this theory.

An evaluation of the results of night vision testing should always be regarded with due consideration. It should be borne in mind that some of the tests are conducted at the bare thresholds of visibility and that a subject's responses may be influenced by his intelligence, by learning and by a host of other variables.

45 Young Building

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41 Riddell, W. J. B. Two Clinical Tests for Night Blindness, *Tr. Ophth. Soc. U. Kingdom* **60** 181, 1940.

## DEPTH PERCEPTION AND FLYING ABILITY

SQUADRON LEADER LEO S S KIRSCHBERG  
MEDICAL BRANCH, ROYAL CANADIAN AIR FORCE

THE TERMS "ocular muscle balance" and "depth perception" have been much abused during the past five years. They have become common terms, especially in the air forces of all nations, and have thereby presented a confused problem to many ophthalmologists who have been asked to examine young men desirous of becoming air force pilots. The terms "ocular muscle balance" and "depth perception" have been used synonymously by persons not fully informed, and the significance of the state of the ocular muscle balance in relation to depth perception and to flying ability has been a source of worry to medical officers of the air forces. The Royal Canadian Air Force during the past few years has tried to solve this problem, this paper presents a summary of some of the results of various studies which it has carried out.

The study was made at a medical selection board of the Royal Canadian Air Force to determine (*a*) the value of a modification of the Verhoeff instrument for measuring acuity of stereopsis, (*b*) the correlation between readings on this instrument and visual acuity, (*c*) the correlation between determinations with this instrument and tests of fusion and ocular muscle balance, (*d*) the significance of measurements of depth perception in selection of personnel to be trained as pilots and (*e*) associated observations regarding visual acuity orthophoria, fusion and pilot training.

The literature both on depth perception per se and on the significance of depth perception in aviation is confused and beset with contradictions. As a prelude to the present study, a review was made of what has been written about depth perception. It is not the purpose of this paper to give a detailed report of this review, but reference must be made to some of the main points of discussion.

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A discussion on this paper was published in the March 1946 issue of the ARCHIVES, page 316.

Report to the Subcommittee on Personnel Selection of the Associate Committee on Aviation Medical Research, National Research Council, Canada Dec 15, 1944, and read in part at the annual meeting of the Canadian Ophthalmological Society, Montreal, June 15, 1945.



## SURVEY OF LITERATURE

*Convergence*—This function ranks high in the list of factors said to be of importance in depth perception. Peter<sup>1</sup> placed great stress on this function, stating, "Both [binocular and monocular] forms of vision are assisted by the same factors, the great efficiency of binocular vision being due largely to convergence," and, later, "The most important factor in the estimation of depth is that of convergence." Despite such dogmatic statements as these, evidence has accumulated whereby one questions the significance of convergence. Walls<sup>2</sup> stated "According to Lindsay Johnson and Elliot Smith, no non-simian mammal can converge its eyes", yet no one will deny that many four-legged animals apparently have excellent depth perception. Walls<sup>3</sup> summed up the significance of convergence in the following manner:

For the estimation of distances in the visual field, convergence must be allowed and it must be allowed to "play" or vary back and forth until it finds its dead center on the object. But the perception of solidity is literally lightning fast [and] does not depend upon a play of convergence, for no time is allowed for that process.

Duke-Elder<sup>4</sup> expressed a similar thought in slightly different fashion:

To maintain that the influence either of the external or of the internal muscles is a predominant factor in the localization of depth is impossible, for objects which are illuminated for a period well within the latent period of muscular contraction are seen in relief. Thus [it was] found that depth could be appreciated with practically instantaneous flash illumination, which was estimated by Volkman to be of the order of 0,000,001 second and the reaction time of muscle is much slower than this 0.162 to 0.170 second. It would thus appear that, in the appreciation of depth, the external musculature by its control of the ocular movements has little influence, and that the movements of accommodation and convergence play only a small part and form an extremely unreliable guide.

Despite this dogmatic statement by so eminent an authority, at the outbreak of the present war practically every air force in the world did maintain just this, and the results of tests for ocular muscle balance were considered as important factors in the selection of candidates for pilot training.

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1 Peter, L. C. *Extra-Ocular Muscles*, Philadelphia, Lea & Febiger, 1941, pp 78-79.

2 Walls, G. L. *Vertebrate Eye*, Bloomfield Hills, Mich., Cranbrook Press, 1942, p 312.

3 Walls,<sup>2</sup> p 315.

4 Duke-Elder, W. S. *Text-Book of Ophthalmology*, London, Henry Kimpton, 1933, vol 1, p 1065.

*Accommodation*—This factor no longer is considered as significant as it once was, indeed, many authors (Adler,<sup>5</sup> Duke-Elder<sup>4</sup> and Walls<sup>6</sup>) have stated that accommodation is either relatively or entirely unimportant

That the presence of orthophoria or of heterophoria has, respectively, a good or a bad effect on depth perception has been contended for a long time. This theory also is losing supporters as the evidence against it grows. Duke-Elder<sup>7</sup> stated

the theory advanced by many of the older thinkers that stereoscopic vision was based on muscular movements, cannot be upheld. It depends on the stimulation of disparate retinal points.

The work of Elliot<sup>8</sup> is extremely significant

The presence of orthophoria or of heterophoria did not affect the stereoscopic vision as measured by the Rotating Depth Perception apparatus on 222 airmen and the Rotating Stereogram on 146 airmen

In considering depth perception and flying ability, a fundamental concept on which the standards of ocular muscle balance of the Royal Air Force and the Royal Canadian Air Force have been based is that the presence of heterophoria exercises a detrimental effect on depth perception. Parsons,<sup>9</sup> in quoting the Air Force standards, stated

It has now been proved beyond argument that lack of true ocular muscle balance is the most common cause of error in judgment in bringing an aircraft to the landing ground. It has been shown that Exophorics tend to flatten out their aircraft too early, having judged the ground to be nearer than it actually is, conversely, Esophorics are inclined to fly into the ground

Elliot<sup>10</sup> was not able to confirm this, for in a study of 175 ceased training student pilots with landing difficulty, whether the error was in leveling off too high or in flying into the ground was not related to the type of heterophoria (i.e., to either the exophoric or the esophoric tendency). Regarding the vergence of visual axes, Duke-Elder<sup>4</sup> commented

If prisms, base in, are placed in front of each eye, objects do not seem much farther away even although the visual axes diverge, nor with prisms base out do they appear very much nearer

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5 Adler, F. H. *Clinical Physiology of the Eye*, New York, The Macmillan Company, 1933, p. 236

6 Walls,<sup>2</sup> p. 313

7 Duke-Elder,<sup>4</sup> p. 1079

8 Elliot, A. J. Report to the Director of Medical Services, R C A F, Nov 2, 1942, p. 22

9 Parsons, J. J. *Diseases of the Eye*, London, J & A Churchill, 1938, p. 674

10 Elliot<sup>8</sup> p. 21

The difference between an examining room and man's usual environment has been noted by Adler,<sup>11</sup> who remarked

a person with one eye has very much less depth perception than an individual with normal binocular vision, at least when tested under such strict conditions [an ophthalmic examination room] It is equally true that under natural conditions the one-eyed individual can judge depth of objects and speed of movement surprisingly well

Ballantyne<sup>12</sup> also noted

It seems impossible to conceive of clinical or laboratory tests which could estimate the capacity of the pilot to meet such conditions as landing speed of the aircraft, nature of the landing ground, etc

Apparently, no official cognizance has been taken of the newer opinions, for the Consultant Oculist to the Royal Air Force, Air Commodore Livingston,<sup>13</sup> in a recent discussion of visual problems in aerial warfare, did not show any great deviation from the Air Force views of the past

It is the aim of the present study to show that a reliable measure of depth perception has been obtained and to correlate this method of measurement with other ocular examinations, ultimately correlating all the ocular tests with the ability of aircrew trainees to learn to fly

#### METHODS

Much of the following data was obtained from the examination of 707 aircrew trainees forming eight consecutive courses at an initial training school of the Royal Canadian Air Force Aircrew chosen for trades other than pilot or dropped from training for nonflying reasons were eliminated from the flying ability correlation study, the remainder were followed through both elementary and advanced flying training until they either won their wings or were dropped from training for flying reasons Progress reports were received from the nine primary and eighteen advanced flying training schools training the student pilots in this project, of the original 707 trainees only 471 actually received full pilot training and either received their wings or were dropped from training because of poor flying ability The 236 airmen eliminated from the final study did not receive pilot training because of selection for aircrew trades other than pilot, sickness or injury necessitating hospitalization and loss of time beyond the duration of this study, an sickness failure in ground instruction or death

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11 Adler,<sup>5</sup> p 235

12 Ballantyne, A J Glasgow M J **133** 73, 1940

13 Livingston, P C Lancet **2** 67, 1944

An original instrument for measuring acuity of stereopsis was described in 1942 by Verhoeff<sup>14</sup>. A model was constructed according to the prescribed measurements, it was found to have two drawbacks. First, it was too small, and, second, if held in the hand as directed, it was too unsteady. Accordingly, a modification of the original instrument was constructed of wood, three times the size of the original, the main differences between the Verhoeff and the R C A F instrument are (a) The new unit is three times the size of the original, and the working distance is 3 meters, (b) the new unit is of solid wood construction and rests on a table, giving it more steadiness than a cardboard unit held in the examiner's hand, (c) Verhoeff's instrument was advanced toward the subject until, eight successive correct answers were obtained, and the score recorded depended on this distance, whereas the procedure in the present study stipulated that both the instrument and the subject remain stationary, thus eliminating such factors as motion parallax. The depth perception score was recorded as the number of correct answers out of a possible eight, inasmuch as eight different test panels were shown to the subject.

The other ocular measurements familiar to ophthalmologists were made. Visual acuity was tested with the American Optical Company's Project-O-Chart, the heterophorias were measured with the Maddox rod at 6 meters, and fusion was examined in two ways. (a) The desire for, or tendency to, fusion was tested with the Harman Diaphragm, and (b) the amplitude, or range of fusion, i. e., abduction plus adduction, was determined with the Worth Amblyoscope. The method of use of the various test instruments and the normalcy or otherwise of the results are recorded in the R C A F Service publications<sup>15</sup>.

In appraisal of the depth perception instrument, 10 subjects were examined repeatedly to demonstrate the test-retest reliability of the measure. Similarly, a small group was tested repeatedly, both binocular and monocular tests being made, to demonstrate the difference between binocular and monocular impressions, 248 binocular and 496 monocular determinations were made for this purpose.

Through the excellent cooperation of the medical officers at the flying training schools, liaison was established with these units, and, although the student pilots were posted to all parts of Canada, documentary evidence was obtained in the case of each trainee and details of his ultimate disposal were thus collected. Of the 504 airmen

14 Verhoeff, F. H. Simple Quantitative Test for Acuity and Reliability of Binocular Stereopsis, *Arch. Ophth.* 28:1000 (Dec.) 1942.

15 Medical Examination and Selection of Aircrew Personnel, Canadian Air Publication 195, 1942, vol. 9, pt. 2.

tested with the depth perception instrument, data for 201 are not included in the flying ability correlation study, for reasons already stated, conclusions will, accordingly, be based on the data for 303 airmen. A larger group of airmen was obtained for the other ocular studies, e g, determinations of visual acuity, heterophoria and fusion, reports concerning these tests will be made on 471 airmen.

## RESULTS

### DEPTH PERCEPTION

*The Instrument*—In reviewing the literature on stereopsis, it was noticed that in many cases in which depth perception instruments were used no figures were offered to show whether or not the instrument gave repeatable results, it was felt that retest reliability is an essential

TABLE 1—*Test-Retest Reliability of the Depth Perception Instrument for Ten Subjects Tested Ten Times Each*

| Case Number            | Scores on 10 Examinations |   |   |   |   |   |   |   |   |   | Average Score | Average Deviation | Standard Deviation |
|------------------------|---------------------------|---|---|---|---|---|---|---|---|---|---------------|-------------------|--------------------|
|                        |                           |   |   |   |   |   |   |   |   |   |               |                   |                    |
| 1                      | 5                         | 6 | 7 | 7 | 5 | 7 | 7 | 7 | 7 | 7 | 6.5           | $\pm 0.70$        | $\pm 0.81$         |
| 2                      | 7                         | 6 | 6 | 6 | 6 | 6 | 5 | 6 | 6 | 7 | 6.1           | $\pm 0.36$        | $\pm 0.54$         |
| 3                      | 4                         | 5 | 5 | 5 | 5 | 4 | 5 | 4 | 4 | 4 | 4.5           | $\pm 0.50$        | $\pm 0.50$         |
| 4                      | 3                         | 3 | 4 | 4 | 5 | 5 | 6 | 6 | 7 | 6 | 4.9           | $\pm 1.12$        | $\pm 1.30$         |
| 5                      | 4                         | 5 | 4 | 5 | 5 | 4 | 5 | 5 | 6 | 5 | 4.8           | $\pm 0.48$        | $\pm 0.60$         |
| 6                      | 5                         | 4 | 4 | 5 | 5 | 5 | 4 | 4 | 5 | 4 | 4.5           | $\pm 0.50$        | $\pm 0.50$         |
| 7                      | 4                         | 3 | 6 | 4 | 4 | 5 | 4 | 6 | 5 | 4 | 4.5           | $\pm 0.80$        | $\pm 0.92$         |
| 8                      | 4                         | 4 | 3 | 4 | 5 | 5 | 4 | 3 | 3 | 5 | 4.0           | $\pm 0.60$        | $\pm 0.78$         |
| 9                      | 3                         | 3 | 4 | 3 | 3 | 4 | 3 | 3 | 4 | 4 | 3.4           | $\pm 0.48$        | $\pm 0.49$         |
| 10                     | 2                         | 3 | 4 | 4 | 3 | 3 | 4 | 4 | 4 | 3 | 3.4           | $\pm 0.60$        | $\pm 0.66$         |
| Average of 10 subjects |                           |   |   |   |   |   |   |   |   |   | 4.66          | $\pm 0.61$        | $\pm 0.71$         |

feature of any instrument used in studying depth perception. With this in mind, a reliability test for repeatability was made on 10 subjects to see how much the depth perception scores for each varied from time to time, each subject was tested ten times, at intervals spread over a period of seven weeks. The results are set forth in table 1, and an analysis of the data shows that the average score was 4.66 (out of a possible 8), the average deviation of a subject's scores from his own mean score  $\pm 0.61$  and the average standard deviation  $\pm 0.71$ . Another way of expressing these results is to say that when a subject completes one test (i e, a series of eight judgments) there are 68 chances in a hundred that the score obtained is within 0.71 point of the real score, such as would be determined by the average of an infinite number of tests, it also indicates that there is only 1 chance in a hundred that the results may be off by as much as 2.13 points. This study demonstrated that the instrument gave repeatable results.

and that a subject's depth perception could be assessed on the basis of a single test. It was decided arbitrarily to divide all airmen in the major study into three groups according to their depth perception score. The men scoring 8, 7 or 6 on the instrument were said to have good depth perception, men scoring 5, 4 or 3 "average" depth perception and those scoring 2, 1 or 0 "poor" depth perception. The test-retest study showed this to be a safe method, and in this manner the instrument could be called a reliable measure.

It having been shown that the instrument was a reliable measure, the next step was to show that it normally measured binocular depth perception and that the binocular performance was superior to the monocular performance. A group of subjects was tested repeatedly, both binocularly and with each eye separately, 248 binocular and 496

TABLE 2—*Comparison of Readings on Depth Perception Instrument in 248 Binocular Examinations and 496 Monocular Examinations*

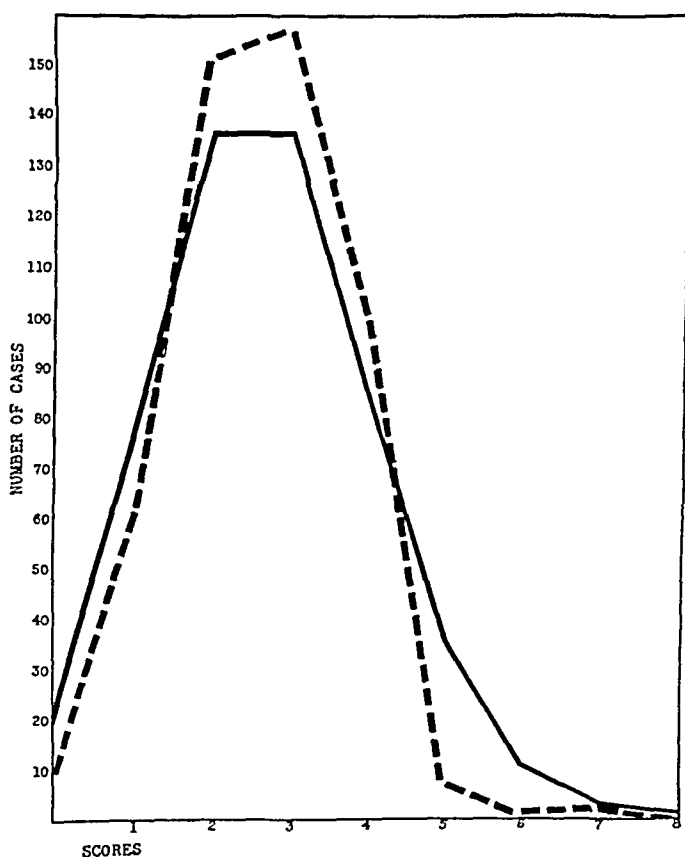
| Score         | Frequency                |                          |
|---------------|--------------------------|--------------------------|
|               | Binocular Determinations | Monocular Determinations |
| 8             | 5                        | 0                        |
| 7             | 19                       | 2                        |
| 6             | 43                       | 1                        |
| 5             | 59                       | 8                        |
| 4             | 74                       | 100                      |
| 3             | 33                       | 159                      |
| 2             | 12                       | 154                      |
| 1             | 2                        | 62                       |
| 0             | 1                        | 10                       |
| Average score | 4.61                     | 2.63                     |

monocular determinations were thus obtained. Table 2 illustrates the superiority of binocular performance (average score, 4.61) over monocular performance (average score, 2.63). To show that there were no reliable monocular clues presented to the subject, a theoretic "pure chance" curve was plotted. This curve was based on guess alone, illustrating this mathematical possibility and representing no depth perception; it is represented in the chart by the continuous line. In the same figure, the broken line represents the curve described by the actual scores made on monocular examination, i. e., the 496 monocular determinations just referred to. The two curves are so similar that there is only one possible conclusion, there were no depth perception factors acting in the monocular determinations. From the data presented in table 2 and in the chart it is reasonable to conclude that the depth perception instrument measures binocular depth perception.

*Depth Perception and Visual Acuity*—In a group of 303 student pilots, a correlation was made between depth perception scores and visual acuity. The results recorded in table 3 show that with normal (20/20) vision in each eye the distribution curve was "normal," i. e., there were equal numbers at each extreme, with the majority of subjects

TABLE 3—*Visual Acuity and Depth Perception*

| Visual Acuity              | Depth Perception Score Group |         |      |
|----------------------------|------------------------------|---------|------|
|                            | Good                         | Average | Poor |
| 20/20 in each eye          | 50                           | 142     | 50   |
| Less than 20/20 in one eye | 10                           | 33      | 18   |
| 20/30 or less in both eyes | 2                            | 15      | 10   |



Theoretic pure chance curve (solid line) based on guess alone compared with the curve for monocular determinations on the depth perception instrument (broken line)

in the group with average depth perception. With visual acuity in one eye less than 20/20 there were twice as many in the group with poor depth perception as in the group with good depth perception, while among the subjects with visual acuity of 20/30 or less in each eye there were five times as many with poor depth perception scores as

with good depth perception scores. Because of the rather small group with vision below 20/20 in each eye, a dogmatic conclusion cannot be drawn, there is none the less a strong indication that good visual acuity is an important factor in depth perception.

*Depth Perception and Fusion*—Amplitude of fusion, measured with the Worth Amblyoscope, was compared with the performance on the depth perception instrument in a group of 504 aircrew trainees. The airmen were divided into four groups according to their amplitude of fusion, and from table 4 it is seen that the average depth perception score was essentially the same for all four groups, thus showing that amplitude of fusion and depth perception scores are independent of each other, this lack of relationship is in keeping with the observations of Junker<sup>16</sup>

Harman<sup>17</sup> described his instrument for measuring the ocular poise, or a subject's desire for fusion, almost thirty-five years ago, it is used

TABLE 4—*Amplitude of Fusion and Depth Perception*

| Degrees of Fusion<br>(Abduction + Adduction) | Number of<br>Airmen | Average Depth<br>Perception Score |
|--|---------------------|-----------------------------------|
| 16 and over                                  | 66                  | 3.7                               |
| 11 to 15                                     | 163                 | 3.8                               |
| 6 to 10                                      | 210                 | 3.7                               |
| 0 to 5                                       | 65                  | 3.9                               |
| Total  | 504                 | 3.7                               |

in the Air Force routine aircrew medical examination with the following standards of ocular poise scale reading. Zero to 3 is "normal", 3 to 6 is "borderline," and above 6 is "cause for rejection." These standards, as well as the details of using the instrument, differ somewhat from those originally outlined by Harman. That a relationship does exist between the amplitude of fusion as measured with the Worth Amblyoscope and the desire for fusion as measured with the Harman Diaphragm is shown in table 5, from which it is seen that as the amplitude of fusion becomes less the Harman Diaphragm readings become higher, i. e., poorer.

The depth perception instrument scores were compared with the test readings with the Harman Diaphragm in a group of 303 student pilots, but no dogmatic conclusion could be drawn from the data, as summarized in table 6. Among those with ocular poise scale readings beyond the strict limits of normal, there were twice as many in the group with poor stereopsis as in the group with good stereopsis, this

<sup>16</sup> Junker, H. Arch. f. Ophth. **142**:367, 1942.

<sup>17</sup> Harman, N. B. Ophthalmoscope **8**:495, 1910.



apparent relationship is not borne out, however, on examining the "ideal" Diaphragm test performers (airmen with readings at 0), for exactly equal numbers were in the group with good and the group with poor depth perception scores. It is felt that were there any decided relationship there would be a higher incidence of "ideal" Diaphragm test performers in the group with good depth perception.

TABLE 5—*Amplitude of Fusion and Desire for Fusion*

| Degrees of Fusion<br>(Abduction + Adduction)<br>(Worth Amblyoscope) | Number of<br>Airmen | Desire for Fusion<br>(Harman Diaphragm<br>Readings) |
|---|---------------------|---|
| 16 and over   | 66                  | 18  |
| 11 to 15  | 163                 | 19  |
| 6 to 10   | 210                 | 22  |
| 0 to 5  | 65                  | 33  |
| Total   | 504                 | 21  |

*Depth Perception and Heterophoria*—Aircrew medical examination in the Air Force includes testing the state of the ocular muscle balance with the Maddox rod, and the standards as laid down for pilots are as follows. Esophoria to  $4\frac{1}{2}\Delta$ , exophoria to  $3\frac{1}{2}\Delta$  or hyperphoria to  $1\frac{1}{2}\Delta$  is considered within the "normal" range, esophoria of  $4\frac{1}{2}$  to  $6\Delta$ , exophoria of  $3\frac{1}{2}$  to  $5\Delta$  or hyperphoria of  $1\frac{1}{2}$  to  $2\Delta$  is called "border-line," and deviations beyond these limits are listed as "cause for rejection." In the series of 303 student pilots, it was found that the 60 airmen in

TABLE 6—*Depth Perception Scores and Harman Diaphragm Readings*

| Depth<br>Perception<br>Score<br>Groups | Ocular Pulse Readings in Harman Diaphragm Test |          |        |          |        |          |        |          |
|--|--|----------|--------|----------|--------|----------|--------|----------|
|  | Over 3   |          | 0.3    |          | 0      |          | Total  |          |
|  | Number   | Per Cent | Number | Per Cent | Number | Per Cent | Number | Per Cent |
| Good                                   | 6  | 10.0     | 44     | 73.4     | 10     | 16.6     | 60     | 100.0    |
| Average                                | 31   | 12.0     | 122    | 69.6     | 32     | 18.4     | 175    | 100.0    |
| Poor                                   | 13   | 19.1     | 45     | 60.1     | 10     | 14.8     | 68     | 100.0    |

the group with good depth perception scores had an average deviation from orthophoria of  $0.96\Delta$ , the 175 airmen in the group with average depth perception scores an average deviation of  $1.24\Delta$  and the 68 trainees in the group with poor depth perception an average deviation of  $1.16\Delta$ . The Maddox rod test is a rather gross measure, and studies carried out elsewhere in the Royal Canadian Air Force by Minnes, Crawford and Shagass<sup>18</sup> showed that the margin of error in the Maddox rod test

18 Minnes, J. F., Crawford, J. S., and Shagass, C. Report to Sub-Committee on Personnel Selection, Ottawa, Canada, National Research Council of Canada, Nov. 23, 1943.

in order to obtain 90 per cent agreement between two examiners was  $2\Delta$ . In view of the results of these authors, it is apparent that the difference between an average heterophoria of  $0.96\Delta$  and one of  $1.16\Delta$  is negligible. It follows that there was no relationship between depth perception scores and heterophoria as measured with the Maddox rod in the series of 303 student pilots. Moreover, of the same group of 303 airmen, 98 were orthophoric, of the 98 with orthophoria, 24 had good stereoptic scores, 56 average scores and 18 poor scores. Were there any striking relationship between orthophoria and depth perception, one would expect to find the majority of subjects with orthophoria in the group with good stereopsis and few, if any, in the group with poor stereopsis, a condition not found in this series.

*Depth Perception and Flying Ability*—Inasmuch as the ultimate decision in pilot training rests with the ability or inability of the trainee to win his wings, reports were collected on 303 airmen followed from preflight or initial training through flying training. From table 7 it is seen that of the 60 airmen with good depth perception scores 35 won

TABLE 7—*Depth Perception and Flying Performance*

| Depth Perception<br>Score Groups | Obtained Wings |          | Ceased Training |          | Total  |          |
|----------------------------------|----------------|----------|-----------------|----------|--------|----------|
|                                  | Number         | Per Cent | Number          | Per Cent | Number | Per Cent |
| Good                             | 35             | 58.3     | 25              | 41.7     | 60     | 100.0    |
| Average                          | 98             | 56.0     | 77              | 44.0     | 175    | 100.0    |
| Poor                             | 42             | 61.8     | 26              | 38.2     | 68     | 100.0    |

their wings and 25 were dropped from training for poor flying ability, while in the comparable group of 68 trainees with poor scores, 42 won their wings and 26 were dropped from training. This shows a complete lack of relationship between depth perception scores and flying ability, for 58.3 per cent of the airmen with good depth perception obtained their wings but a slightly higher percentage (61.8) of the group with poor depth perception also became air force pilots. Similarly, poor depth perception is not related to flying failure, for a higher percentage (41.7) of airmen with good stereopsis were dropped from training for poor flying ability than the percentage (38.2) of trainees with poor depth perception scores.

From these results, it is logical to conclude that because the incidence of successful pilot training and that of failure in training are so similar in both the group with good and the group with poor depth perception scores the measurement of binocular stereopsis bears no relationship to flying performance in a training program such as the British Commonwealth Air Training Plan.

## VISUAL ACUITY AND FLYING ABILITY

It has already been shown that, even though it could not be definitely proved, there is a strong indication that good visual acuity is an important factor in depth perception. Visual acuity was compared with flying performance in a series of 471 student pilots. Data summarized in table 8 show that airmen with 20/20 vision in each eye had a much better prognosis for ability to fly than was the case of airmen with limited visual acuity, for the ratio of success to failure changed from 59.2:40.8, in the group with normal vision, to 50:50, in the group with "one eye less than normal" and there was a complete reversal of ratio (37.2:62.8) in the group with limited vision in both eyes. A limitation of this study is that trainees with really poor vision e. g., in the neighborhood of 20/60, could not be studied, for at the time that this thesis was undertaken very few airmen with visual acuity of less than 20/40

TABLE 8—*Visual Acuity and Flying Performance*

| Visual Acuity              | Obtained Wings |          | Ceased Training |          | Total  |          |
|----------------------------|----------------|----------|-----------------|----------|--------|----------|
|                            | Number         | Per Cent | Number          | Per Cent | Number | Per Cent |
| 20/20 in each eye          | 221            | 59.2     | 152             | 40.8     | 373    | 100.0    |
| Less than 20/20 in one eye | 49             | 50.0     | 49              | 50.0     | 98     | 100.0    |
| 20/30 or less in both eyes | 16             | 37.2     | 27              | 62.8     | 43     | 100.0    |

were being trained as pilots. In an attempt to give aircrew trainees every possible aid, the Royal Canadian Air Force issued to student pilots with defective vision flying goggles incorporating corrective lenses, as determined by cycloplegic refraction. However, because of mechanical or engineering difficulties inherent in the goggles, as well as a strong prejudice among aircrew against aircrew trainees wearing corrective goggles, the vast majority of student pilots did not wear their correction. Indeed, in the series under study only 2 airmen wore corrective goggles, 1 had unaided vision of 20/30 and 20/40 and the other, of 20/60 and 20/50, with correction they had vision of 20/20 + in each eye. Both trainees successfully flew primary type aircraft but were dropped from training at the advanced flying training stage being unable to master faster service aircraft. Despite the aforementioned limitations the study definitely shows that limited visual acuity lowers the chances of a trainee's becoming an Air Force pilot.

## FUSION (HARMAN DIAPHRAGM TEST) AND FLYING ABILITY

Whereas the results for the correlation of depth perception scores with Harman Diaphragm readings were somewhat equivocal, there is no doubt as to the lack of significance of Harman Diaphragm readings for flying performance. From table 9 it is seen that with all types of

Harman Diaphragm performances, i e, in any ocular poise scale reading group, the incidence of successful and of unsuccessful student pilots was almost the same. In this series of 471 student pilots the Harman Diaphragm test was not of any prognostic value in estimating the ability or inability to learn to fly.

TABLE 9—*Harman Diaphragm Test and Flying Performance*

| Harman Diaphragm Test<br>Ocular Poise Scale Reading | Obtained Wings |          | Ceased Training |          |
|---|----------------|----------|-----------------|----------|
|   | Number         | Per Cent | Number          | Per Cent |
| Zero (ideal)  | 52             | 19.3     | 40              | 19.9     |
| 0.3 (normal)  | 183            | 67.8     | 133             | 66.2     |
| 3.6 (borderline)                                    | 32             | 11.8     | 25              | 12.4     |
| 6 and over (cause for rejection)                    | 3              | 1.1      | 3               | 1.5      |
| Total   | 270            | 100.0    | 201             | 100.0    |

## OCULAR MUSCLE BALANCE AND FLYING ABILITY

It has already been shown that no striking relationship between orthophoria and superior depth perception could be demonstrated, in comparing orthophoria with flying performance, of 270 trainees who won their wings 35.9 per cent were orthophoric, and of 201 trainees who were dropped from training for poor flying ability 33.3 per cent were orthophoric, these percentages are so similar that surely the presence of orthophoria is of no significance whatever in actual flying performance.

TABLE 10—*Ocular Muscle Balance and Flying Performance*

| State of Ocular Muscle Balance  | Obtained Wings |          | Ceased Training |          |
|---|----------------|----------|-----------------|----------|
|   | Number         | Per Cent | Number          | Per Cent |
| Maddox rod orthophoria<br>Diaphragm test 0  | 3              | 1.7      | 8               | 6.3      |
| Maddox rod orthophoria<br>Diaphragm test 0.3  | 49             | 28.0     | 28              | 21.6     |
| Maddox rod esophoria to $4\frac{1}{2}\Delta$ , exophoria to $3\frac{1}{2}\Delta$ or<br>hyperphoria to $1\frac{1}{2}\Delta$<br>Diaphragm test 0.3            | 99             | 56.6     | 70              | 54.7     |
| Maddox rod esophoria over $4\frac{1}{2}\Delta$ , exophoria over $3\frac{1}{2}\Delta$ ,<br>or hyperphoria over $1\frac{1}{2}\Delta$<br>Diaphragm test over 3 | 24             | 13.7     | 22              | 17.2     |
| Total   | 175            | 100.0    | 128             | 100.0    |

It is a practice in the Royal Canadian Air Force to consider various ocular muscle balance tests together, and with this in mind the results for the Harman Diaphragm test and for the Maddox rod test were considered together and the data summarized in table 10. Were there any striking relationship between the state of the ocular muscle balance as measured in a medical examining room and the ability to learn to fly, one would expect to find a high incidence of "obtained wings" among

the men with orthophoria and a low incidence among the men with heterophoria. By the same token, one might expect to find a high incidence of "ceased training" among the heterophoric trainees and a low incidence among the orthophoric trainees. This is decidedly not the case. In table 10, there is no essential difference between the percentage of success and that of failure in any of the four groups (except perhaps in the first, or "ideal," group, which is actually too small to permit any definite conclusion). In this series of 303 airmen there was

TABLE 11—*Analysis of Records of 3,684 Student Pilots*

|   |                |       |
|---|----------------|-------|
| Total number of student pilots sent to flying schools   |                | 3,684 |
| Student pilots ceased training at flying schools  | 974 airmen, or | 26.4% |
| Student pilots at flying schools with ocular muscle balance beyond strict "normal" limits                       |                | 78    |
| Student pilots with ocular muscle balance beyond strict "normal" limits dropped from training at flying schools | 21 airmen, or  | 26.9% |

no significant relationship between the results in the ophthalmic examination room and the actual performance in aircraft.

It has already been stated in this report that, because of existing ocular muscle balance standards prerequisite to pilot training, few men with muscle imbalance of a more severe degree were permitted to be trained as pilots. In an effort to obtain a larger series of cases of muscle

TABLE 12—*Analysis of Records of 78 Student Pilots with Ocular Muscle Balance Beyond Normal*

|   |               |       |
|---|---------------|-------|
| Number of student pilots at flying schools with ocular muscle balance beyond strict "normal" limits             |               | 78    |
| Student pilots with ocular muscle balance beyond strict "normal" limits dropped from training at flying schools | 21 airmen, or | 26.9% |
| Number of student pilots at flying schools with "borderline"* ocular muscle balance                             |               | 43    |
| Student pilots in this category who were dropped from training  | 17 airmen, or | 39.6% |
| Number of student pilots at flying schools with "abnormal" ocular muscle balance†                               |               | 35    |
| Student pilots in this category who were dropped from training  | 4 airmen, or  | 11.4% |

\* Examples of "borderline" ocular muscle balance: heterophoria of 5Δ, Harman Diaphragm test reading at 5, convergence or accommodation beyond the average for the airmen's age.

† Examples of "abnormal" ocular muscle balance: heterophoria beyond 6Δ, neglect, Harman Diaphragm test reading beyond 6 or cover test with no recovery.

These examples result from present R C A T standard.<sup>16</sup>

imbalance, the records of 5,603 trainees were reviewed, of whom 3,684 received pilot training. Of this large number, 78 had ocular muscle balance readings beyond the strict limits of "normal" as laid down for the Royal Canadian Air Force. From table 11 it is seen that the rate of "dropped from training" for poor flying ability was essentially the same for the 78 trainees with muscle imbalance (26.9 per cent) as for the whole series of 3,684 trainees (26.4 per cent). Further analysis of the data for the 78 airmen, as represented in table 12, shows that of

35 student pilots with definitely abnormal ocular muscle balance, e g, neglect, exophoria greater than  $6\Delta$ , ocular poise readings beyond 6 in the Harman Diaphragm test or no recovery in the cover test, 31 became Air Force pilots, and only 4 (11.4 per cent) could not learn to fly. These results serve as strong corroborative evidence to support the conclusion reached in the present project, i e, that there was no significant relationship between the readings in the ophthalmic examination room as regards the state of the ocular muscle balance and the actual performance in aircraft.

### SUMMARY AND CONCLUSIONS

A test-retest reliability study made with a modification of the Verhoeff instrument for measurement of stereopsis showed that the instrument gave a reliable indication of the subject's depth perception and that in a single test a subject's binocular depth perception could be categorized as "good," "average" or "poor." It was unlikely that a subject might jump from one category to another, as the average deviation was  $\pm 0.61$  and the average standard deviation  $\pm 0.71$ .

It was shown that the instrument was a measure of binocular depth perception and that there were no successful monocular clues active in the situation as presented to the subject, it was also demonstrated that monocular performance on the instrument was the same as guess or pure chance.

In a series of 303 student pilots there was a strong indication that good visual acuity is an important factor in depth perception.

In a series of 504 aircrew trainees it was shown that amplitude of fusion and depth perception scores were independent of each other.

In a series of 504 airmen it was shown that there was a relationship between the performance on the instrument used to measure amplitude of fusion (Worth Amblyoscope) and the instrument used to determine desire for fusion (Harman Diaphragm).

In a series of 303 student pilots it was not possible to demonstrate any definite relationship between desire for fusion and depth perception scores.

In a series of 303 student pilots there was no relationship between depth perception scores and heterophoria as measured with the Maddox rod. Moreover, in a series of 98 trainees with orthophoria it was not possible to demonstrate any relationship between orthophoria and superior depth perception.

In a series of 303 student pilots there was a complete lack of relationship between depth perception and flying ability as shown by successful graduation or by failure in the pilot's course of the British Commonwealth Air Training Plan.

In a series of 471 student pilots it was shown that an airman with 20/20 vision in each eye had a much better prognosis for ability to learn to fly than had the airman with less acute sight

In the same series of 471 airmen desire for fusion as measured with the Harman Diaphragm test was of no prognostic value in estimating the ability to learn to fly

In the series of 471 airmen it was also demonstrated that the finding of orthophoria on examination with the Maddox rod had no bearing on flying ability

In a series of 303 airmen the results of the Harman Diaphragm and Maddox rod tests were considered together, and it was found that no significant relationship existed between the readings in the ophthalmic examining room and the actual performance in aircraft

In reviewing the records of 3,684 student pilots and those of a group that included 78 trainees with readings for ocular muscle balance beyond the strict limits of "normal" according to air force standards, it was found that the rates of failure in training were almost identical in the two groups. Moreover, a subgroup of 35 airmen with definite muscular imbalance had a much lower rate of failure in training, thus showing that with the present limits or standards there is no correlation between the ophthalmic readings and the ability of the student pilot to win his wings

# CLINICAL ASPECTS OF STEREOPSIS

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THE present work was undertaken in an attempt to throw further light on the subject of depth perception as it is related to aviation. A considerable amount has been written on the theoretic and laboratory aspects of this subject, but articles giving clinical analyses of cases have been few. An interesting series of cases was published by Howard in 1919<sup>1</sup>. That author described in detail the apparatus he used for the testing of depth perception and then presented a series of cases with a careful analysis and discussion of the results. It is felt that further clinical surveys are indicated in an effort to extend knowledge of the significance which can be attached to results obtained from tests of depth perception. This paper, therefore, presents a series of cases and tries to interpret the results of tests for depth perception in the light of other tests used and of certain clinical experiments which will be described.

A test for acuity of stereopsis was used in this study as the measure of accuracy of depth perception. This test is somewhat different from those usually employed and will be described in detail. Also, it was found necessary to devise a test for the quantitative estimation of the degree of suppression. The latter test will be described in detail.

As the work progressed, it divided itself into three parts. The first part consisted in a study of 246 clinical cases in which acuity of stereopsis was tested. The results obtained from these cases indicated that important relationships existed between refractive errors and stereoptic acuity. Therefore the second part of the study was undertaken, which consisted in the testing of trained subjects for acuity of stereopsis in whom various refractive errors had been induced with lenses placed before the eyes. Finally, to illuminate further the observations on the original series and to show the variable factors present in the test for stereopsis, the third part of the study was carried out. This consisted in testing trained subjects in order to determine the variations in acuity of stereopsis caused by changing the size and separation of the test objects employed.

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<sup>1</sup> Howard, H. J. A Test for the Judgment of Distance, *Am J Ophth* 2:656-675, 1919

<sup>2</sup> Footnote deleted by author



## APPARATUS AND METHODS

The apparatus and methods employed were essentially the same for all parts of the investigation and may be described now

1 Acuity of stereopsis was tested with the synoptophore (Clement Clarke) A series of 6 slides was designed so as to allow a quantitative estimation of acuity of stereopsis Each slide presented two round black dots, which were seen against the white, ground-glass screen of the instrument The working distance of the instrument was approximately 156 cm, and the dots were made so as to appear horizontally separated by 25, 26, 26½, 27, 27½ and 28 minutes of arc and to have a diameter of 3 minutes each The slide having a separation of 25 minutes was employed as a standard before one eye, while one of the other slides was used before the other eye The slides used for comparison, then, represented increases of separation of 1, 1½, 2, 2½ and 3 minutes Since visual acuity readings with the Snellen chart are based on an angle of 1 minute, it was decided, for the sake of convenience, to convert levels of stereoptic acuity into figures similar to readings for visual acuity, namely, stereoptic acuities of 20/20, 20/30, 20/40, 20/50 and 20/60

The slides used in the third part of the work, to determine effect of size and separation of the dots on acuity of stereopsis, formed 5 series of 6 slides each They were similar to the slides already described and can be summarized in the following tabulation

|                                     | Diameter of Dots, Min | Separation of Dots     |
|-------------------------------------|-----------------------|------------------------|
| Slides to Test Effect of Size       |                       |                        |
| Series small                        | 3                     | 50 minutes as standard |
| Series medium                       | 6                     | 50 minutes as standard |
| Series large                        | 9                     | 30 minutes as standard |
| Slides to Test Effect of Separation |                       |                        |
| Series medium                       | 3                     | 50 minutes as standard |
| Series wide                         | 3                     | 75 minutes as standard |

All levels of stereoptic acuity for these 5 series of slides were converted to readings of 20/20, 20/30, 20/40, 20/50 and 20/60, as described in a previous paragraph

The slides were made by photographing drawings, at the proper reduction in size, and reproducing positive prints on clear film The same technics of photography, development and printing were used for each slide When the slides were made, measurement of the dots indicated that the basic angle was approximately 57, instead of 60, seconds This error was ignored

With all these series of slides, the test consisted in finding the best stereoptic acuity which the subject could attain The standard slide and one with a chosen separation of the dots were presented, one before each eye The subject was given fifteen seconds and then was asked to tell which dot appeared the nearer He was instructed to guess, if he did not know, giving "right" and "left" as his only answers The procedure was then repeated, 5 random choices being given In assessment of his score, 5 correct answers out of 5 choices constituted a pass, and 3 out of 5, a failure If 4 correct answers out of 5 choices were given, the choices went on to 10 and 9 correct answers out of 10 choices was a pass and 8 or less correct answers a failure Testing was continued using slides of different separations until the highest level of stereoptic acuity for which a pass could be attained had been found

If, however, the subject's stereopsis was too poor to be assessed by the dot test, a pair of slides which gave the impression of depth from a small eccentric

circle inside a larger circle was used. Successful appreciation of depth using this target was recorded as "circles," and failure, as "nil."

2 Suppression was tested by means of the synoptophore. The two slides used were made by photographing, reducing and printing a Snellen chart on clear film. The Snellen chart was reduced so that the letters subtended the same angle in the synoptophore that they did in the chart at 20 feet (6 meters). A letter was missing from each of the lines in one slide, and a different letter, from each of the lines in the other slide. The two reduced Snellen charts were presented, one before each eye. The subject was asked to read the fused charts, and if any of the letters which were present before one eye only were not seen this was noted. Suppression was graded as the largest letter which was not seen and was charted as 20/20, 20/30, 20/40, 20/60, 20/80 and 20/120, corresponding to the size of that letter.

3 Other examinations included manifest refraction, followed by refraction with homatropine cycloplegia, external examination of the eyes, examination of the fundus, the cover test and Maddox rod readings for near and distant vision, tests for objective convergence, with a small light used as object, and accommodation. Additional examinations were used as seemed indicated in particular cases. Visual acuity was tested both with the American Optical Company Project-O-Chart at 20 feet and with the synoptophore.

## RESULTS

### I CLINICAL STUDY

This part of the work consisted in the study of a series of 246 patients who were seen in consultation in the Royal Canadian Air Force. They were first tested for acuity of stereopsis and suppression and then were given an ophthalmic examination. The results are presented in the form of a graph.

The graph shows the visual acuity of the poorer eye, as tested with the synoptophore, charted against acuity of stereopsis. The subjects are represented by crosses, except for those who showed certain visual peculiarities and who are represented by the various characters employed in the graph. All the cases crowd into the lower right half of the graph, a roughly diagonal boundary separating them from the upper left corner. From this appearance it can be concluded that visual acuity is a limiting factor in stereopsis and that it is impossible for a person with poor visual acuity to have good acuity of stereopsis. Table 1 shows the result when the cases represented by the symbols are removed.

It is now seen that the cases lie mainly along a line running from the lower left to the upper right corner of the table. This suggests that when certain ocular conditions were not present stereoptic acuity varied as visual acuity.

Those visual factors which are represented by the symbols, and which apparently affected stereopsis without changing the visual acuity, are learning, suppression, hypermetropia, anisometropia and cylinder errors at crossed axes.



failure The other 17 patients improved partially or completely to a stereoptic acuity of 20/20 After some experience, it was found possible to predict the cases in which "learning" would be a factor The patients for whom it was significant were characterized by the slowness of their responses at the time of testing However, with practice they gradually began to appreciate depth and became as rapid and as accurate in their judgments as the best subjects The 2 subjects who did not learn readily gave answers which were, however, consistently wrong Their inability to improve seemed to be due to lack of interest or to inferior intelligence The ocular examination did not reveal any other cause for their failure to learn

The cases of "suppression" are collected in the lower right corner of the graph except for the 2 in the 20/20, 20/20 square In these 2 cases the amount of suppression was 20/30 In none of the other cases in which acuity of stereopsis was commensurate with visual acuity did suppression occur The amount of suppression is charted against the acuity of stereopsis in table 2

TABLE 2—*Suppression Versus Acuity of Stereopsis*

| Amount of<br>Suppression | Acuity of Stereopsis |       |       |       |       | Circles | Nil |
|--------------------------|----------------------|-------|-------|-------|-------|---------|-----|
|                          | 20/20                | 20/30 | 20/40 | 20/50 | 20/60 |         |     |
| 20/120                   |                      |       |       |       |       | 6       | 2   |
| 20/80                    |                      |       |       |       |       | 2       |     |
| 20/60                    |                      |       |       |       | 1     |         |     |
| 20/40                    |                      |       |       | 2     | 1     | 2       |     |
| 20/30                    | 2                    | 2     | 1     |       |       |         |     |
| 20/20                    |                      |       |       |       |       |         |     |

It can be seen that the higher degrees of suppression are accompanied with greater lowering of stereoptic acuity Apparently, a quantitative relationship between the amount of suppression and the loss of stereoptic acuity does exist

The symbol for hypermetropia in the graph is used for all subjects with hypermetropia of more than  $+2.50$  D spherical equivalent as determined with homatropine refraction In this graph, the degree of hypermetropia shows no obvious relationship to acuity of stereopsis However, several of the patients having high degrees of hypermetropia associated with lowered accommodation complained of difficulty in maintaining clear fixation on the small dots in the target It was therefore decided to designate with a special symbol all subjects having hypermetropia of over  $+2.50$  D in either eye

A special symbol has been used for all patients having over 0.75 D of hypermetropic anisometropia, as calculated from the spherical equivalents and for 1 patient having over 0.75 D of hypermetropic cylinder error at axes crossed more than 45 degrees In part 2 it will be shown that skilled observers can overcome large refractive errors of these

types To the unskilled observer these errors probably have a significant influence on stereopsis

Anisometropia for all subjects was calculated from the spherical equivalents and is charted against acuity of stereopsis in table 3 No

TABLE 3—*Hypermetropic Anisometropia Versus Acuity of Stereopsis*

| Hypermetropic<br>Anisometropia, D | Acuity of Stereopsis |       |       |       |       |  | "Circles" | "Nil" |
|-----------------------------------|----------------------|-------|-------|-------|-------|--|-----------|-------|
|                                   | 20/20                | 20/30 | 20/40 | 20/50 | 20/60 |  |           |       |
| 1 12                              |                      |       |       |       | 1     |  |           |       |
| 1 00                              |                      |       |       |       | 1     |  | 1         |       |
| 0 87                              |                      | 1     |       |       |       |  |           |       |
| 0 75                              |                      |       |       |       |       |  | 8         |       |
| 0 67                              |                      | 1     | 2     |       |       |  | 1         |       |
| 0 50                              | 4                    | 1     | 3     | 3     |       |  | 3         |       |
| 0 37                              | 5                    | 3     | 1     |       | 3     |  | 6         | 1     |
| 0 25                              | 17                   | 13    | 6     | 2     | 4     |  | 4         | 1     |
| 0 12                              | 17                   | 22    | 5     | 4     | 3     |  | 10        | 3     |
| 0 00                              | 25                   | 20    | 10    | 3     | 3     |  | 10        | 1     |

relationship is evident The subjects were too few to permit our making a separate table for cylinder errors at crossed axes

Tables 4, 5 and 6, in which age, accommodation and convergence are compared with acuity of stereopsis, and tables 7 and 8, in which Maddox rod readings for near and distant vision are compared with

TABLE 4—*Age Versus Acuity of Stereopsis*

| Age, Years | Acuity of Stereopsis |       |       |       |       |  | Circles | Nil |
|------------|----------------------|-------|-------|-------|-------|--|---------|-----|
|            | 20/20                | 20/30 | 20/40 | 20/50 | 20/60 |  |         |     |
| 46-50      | 2                    |       | 1     |       | 2     |  | 2       |     |
| 41-45      | 5                    | 2     | 1     | 2     |       |  | 2       |     |
| 36-40      | 9                    | 8     | 3     |       | 3     |  | 1       | 1   |
| 31-35      | 11                   | 10    | 4     | 2     | 3     |  | 7       |     |
| 26-30      | 18                   | 13    | 8     | 1     | 6     |  | 9       | 1   |
| 21-25      | 21                   | 28    | 11    | 5     | 2     |  | 21      | 4   |
| 15-20      | 6                    | 2     | 1     | 3     | 1     |  | 5       |     |

TABLE 5—*Near Point of Accommodation Versus Acuity of Stereopsis*

| Near Point of<br>Accommodation,<br>Mm | Acuity of Stereopsis |       |       |       |       |  | Circles | Nil |
|---------------------------------------|----------------------|-------|-------|-------|-------|--|---------|-----|
|                                       | 20/20                | 20/30 | 20/40 | 20/50 | 20/60 |  |         |     |
| 170                                   | 1                    | 2     |       |       | 2     |  | 1       |     |
| 160                                   | 3                    | 3     | 1     |       | 2     |  |         |     |
| 150                                   | 5                    | 3     | 2     |       | 1     |  | 2       |     |
| 140                                   | 1                    | 2     | 3     |       |       |  | 1       |     |
| 130                                   | 10                   | 7     |       |       |       |  | 6       |     |
| 120                                   | 9                    | 14    | 5     | 1     | 1     |  | 5       | 1   |
| 110                                   | 12                   | 6     | 5     | 2     | 5     |  | 7       | 1   |
| 100                                   | 10                   | 13    | 4     | 6     | 3     |  | 14      | 3   |
| 90                                    | 4                    | 5     | 3     |       | 1     |  | 6       | 2   |
| 80                                    | 2                    | 1     |       |       |       |  | 2       |     |

acuity of stereopsis, show no apparent correlations Charting of results from using the cover test for near and distant vision against acuity of stereopsis also shows no correlations

During the testing of stereopsis the subjects were given completely random choices. Therefore, the chances of either the right or the left

TABLE 6—*Near Point of Convergence Versus Acuity of Stereopsis*

| Near Point of<br>Convergence, Mm | Acuity of Stereopsis |       |       |       |       | Circles | Nil |
|----------------------------------|----------------------|-------|-------|-------|-------|---------|-----|
|                                  | 20/20                | 20/30 | 20/40 | 20/50 | 20/60 |         |     |
| 60                               | 5                    | 7     |       |       | 1     | 4       |     |
| 70                               | 10                   | 10    | 4     | 3     | 3     | 6       | 2   |
| 80                               | 15                   | 10    | 2     | 4     | 3     | 11      | 1   |
| 90                               | 13                   | 14    | 6     |       | 2     | 4       | 1   |
| 100                              | 9                    | 6     | 8     | 4     | 1     | 12      | 1   |
| 110                              | 6                    | 7     | 2     |       | 2     | 3       | 1   |
| 120                              | 3                    | 2     | 3     |       | 1     | 1       | 1   |
| 130                              | 2                    | 2     | 1     | 1     | 1     | 1       |     |
| 140                              | 2                    | 1     |       |       |       | 3       |     |
| 150                              | 1                    | 3     |       |       | 1     |         |     |

TABLE 7—*Amounts of Heterophoria for Near Vision, as Measured with the Maddox Rod, Versus Acuity of Stereopsis*

| Heterophorias, D | Acuity of Stereopsis |       |       |       |       | Circles | Nil |
|------------------|----------------------|-------|-------|-------|-------|---------|-----|
|                  | 20/20                | 20/30 | 20/40 | 20/50 | 20/60 |         |     |
| Esophoria 6      |                      |       | 1     |       |       | 1       | 1   |
| 5                | 2                    | 3     |       |       |       | 1       |     |
| 4                | 2                    |       |       | 1     |       |         |     |
| 3                | 3                    | 2     |       |       |       | 2       |     |
| 2                | 4                    | 2     | 4     |       | 1     | 2       |     |
| 1                | 4                    | 3     |       |       |       | 1       |     |
| Orthophoria      | 8                    | 3     |       | 2     | 3     | 2       | 1   |
| 1                | 7                    | 4     | 3     |       |       | 4       |     |
| 2                | 8                    | 4     | 1     | 1     | 1     | 2       |     |
| 3                | 3                    | 3     |       | 2     |       | 3       |     |
| 4                | 7                    | 7     | 3     |       | 1     | 6       |     |
| 5                | 2                    | 7     | 2     | 2     | 2     | 1       |     |
| 6                | 4                    | 7     | 5     | 1     | 4     | 5       |     |
| 7                | 2                    | 1     |       |       |       |         |     |
| 8                | 2                    | 3     | 2     | 1     | 1     | 3       | 1   |
| 9                | 1                    | 2     |       |       |       | 1       |     |
| 10               | 2                    |       | 2     |       |       |         |     |
| 11               | 1                    | 1     |       |       |       |         |     |
| Exophoria 12     | 1                    | 1     |       |       |       |         |     |

TABLE 8—*Amounts of Heterophoria, as Determined with the Maddox Rod, Versus Acuity of Stereopsis*

| Heterophorias, D | Acuity of Stereopsis |       |       |       |       | Circles | Nil |
|------------------|----------------------|-------|-------|-------|-------|---------|-----|
|                  | 20/20                | 20/30 | 20/40 | 20/50 | 20/60 |         |     |
| Esophoria 7      |                      | 1     |       |       |       |         |     |
| 6                |                      |       | 1     |       |       | 2       | 1   |
| 5                | 1                    | 1     |       |       |       |         |     |
| 4                | 1                    | 1     | 2     |       | 1     |         | 1   |
| 3                | 3                    | 1     | 1     |       |       | 5       |     |
| 2                | 13                   | 6     | 2     | 1     | 1     | 5       |     |
|                  | 11                   | 6     | 4     | 4     | 2     | 6       |     |
| Orthophoria      | 24                   | 7     | 7     | 5     | 6     | 13      | 1   |
| 1                | 6                    | 3     | 4     |       | 1     | 2       |     |
| 2                | 1                    | 4     | 3     |       |       |         |     |
| 3                | 1                    |       | 1     |       | 1     | 1       |     |
| 4                | 2                    | 1     | 1     |       | 1     |         |     |
| Exophoria 5      |                      | 1     |       |       |       |         |     |

dot appearing nearer were approximately equal. Despite this, some subjects had a differential tendency to choose the dot on one side as

closer than that on the other side. The right dot was usually chosen, although occasionally it was the left. No cause was found for this.

## II EFFECTS OF INDUCED REFRACTIVE ERRORS ON STEREOPTIC ACUITY

*Method*—The second part of this work is a study of the effect of induced refractive errors on acuity of stereopsis in trained subjects. On their first visit, subjects in this group were tested for acuity of stereopsis while wearing their emmetropic correction obtained by manifest refraction. On subsequent days they returned for one hour's testing each day, at which time, with various lenses added to the manifest refraction, the acuity of vision and the acuity of stereopsis were retested.

During the testing it was found difficult to control variations in relaxation of accommodation. This was revealed by moment to moment changes in visual acuity while the subject was wearing plus lenses. To reduce this variable as much as possible, only subjects with a spherical error of less than +1.00 D and subjects who showed little tendency to variations in visual acuity were

TABLE 9—*Visual Acuity Versus Acuity of Stereopsis in Subjects with Induced Myopia in Both Eyes*

| Visual Acuity | Acuity of Stereopsis |       |       |       |       | Circles |
|---------------|----------------------|-------|-------|-------|-------|---------|
|               | 20/20                | 20/30 | 20/40 | 20/50 | 20/60 |         |
| 20/80         |                      |       |       | 1     | 4     | 10      |
| 20/60         |                      |       | 5     | 2     | 3     | 2       |
| 20/40         |                      | 6     | 9     | 2     |       |         |
| 20/30         | 8                    | 23    | 1     |       |       |         |
| 20/20         | 22                   | 5     |       |       |       |         |
| Average       |                      | 20/30 | 20/46 | 20/56 | 20/71 | 20/76   |

accepted. While testing was in progress, visual acuity was repeatedly checked to make sure that no major variations in accommodation were occurring.

The lenses used may be listed as follows: (1) plus spheres in front of both eyes, inducing myopia in both eyes, (2) a plus sphere in front of one eye, inducing myopia in one eye and accompanying anisometropia, (3) plus cylinders at axes 90 and 180 in front of each eye, inducing simple myopic astigmatism at axes 90 and 180 in both eyes, (4) a minus sphere in front of one eye, inducing hypermetropic anisometropia without loss of visual acuity, (5) minus cylinders at axes 90 and 180 in front of each eye, inducing simple hypermetropic astigmatism at axes 90 and 180 in both eyes, and (6) minus cylinders at axis 90 in front of one eye and at axis 180 in front of the other eye, inducing simple hypermetropic astigmatism at crossed axes.

*Observations*—The effects of these various lenses will now be described, in the order given.

Table 9 shows the reduction of visual acuity due to myopia in both eyes charted against acuity of stereopsis. It can be seen that the two variables show a correlation. This table appears similar to table 1 and confirms the observation that when the visual peculiarities mentioned in part I are eliminated acuity of stereopsis shows a direct relation to visual acuity.

In table 10 visual acuity with myopia induced in one eye is charted against acuity of stereopsis. The same analysis applies as in table 9. It is also noted that the average visual acuities for the various levels of stereopsis are about the same in tables 9 and 10. If the acuity of stereopsis depended on the average visual acuity of the two eyes, the averages in table 10 would be about one-half those in table 9. That they

TABLE 10—*Visual Acuity Versus Acuity of Stereopsis in Subjects with Induced Myopia in One Eye*

| Visual Acuity | Acuity of Stereopsis |       |       |       |       | Circles |
|---------------|----------------------|-------|-------|-------|-------|---------|
|               | 20/20                | 20/30 | 20/40 | 20/50 | 20/60 |         |
| 20/120        |                      |       |       |       |       | 1       |
| 20/80         |                      |       |       | 1     | 4     | 8       |
| 20/60         |                      |       | 2     | 3     | 1     | 1       |
| 20/40         | 1                    | 1     | 3     | 5     | 2     | 2       |
| 20/30         | 6                    | 13    | 3     | 2     | 1     |         |
| 20/20         | 5                    | 3     |       |       |       |         |
| Average       |                      | 20/29 | 20/41 | 20/47 | 20/61 |         |

TABLE 11—*Cylinder Error Versus Acuity of Stereopsis for Subjects with Induced Simple Myopic Astigmatism, Minus Cylinder Error at Axis 90*

| Cylinder Error, D | Acuity of Stereopsis |       |       |       |       | Circles |
|-------------------|----------------------|-------|-------|-------|-------|---------|
|                   | 20/20                | 20/30 | 20/40 | 20/50 | 20/60 |         |
| 2.00              |                      |       |       |       | 2     |         |
| 2.50              |                      |       | 1     | 1     | 4     | 3       |
| 2.00              |                      | 1     | 3     | 2     | 6     | 7       |
| 1.50              |                      | 7     | 4     | 2     | 2     | 3       |
| 1.00              | 8                    | 6     | 2     | 3     |       |         |
| 0.50              | 4                    | 7     | 1     |       |       |         |
| 0.00              | 9                    | 1     |       |       |       |         |

TABLE 12—*Cylinder Error Versus Acuity of Stereopsis for Subjects with Induced Simple Myopic Astigmatism, Minus Cylinder Error at Axis 180*

| Cylinder Error, D | Acuity of Stereopsis |       |       |       |       | Circles |
|-------------------|----------------------|-------|-------|-------|-------|---------|
|                   | 20/20                | 20/30 | 20/40 | 20/50 | 20/60 |         |
| 3.50              |                      |       | 2     |       | 1     |         |
| 3.00              |                      |       | 7     |       |       |         |
| 2.50              | 5                    | 2     | 3     |       | 3     | 2       |
| 2.00              | 6                    | 4     | 4     | 1     | 3     |         |
| 1.50              | 10                   | 4     | 3     |       | 1     |         |
| 1.00              | 11                   | 6     | 2     |       |       |         |
| 0.50              | 9                    | 1     |       |       |       |         |

are similar indicates that the acuity of stereopsis depends on the visual acuity in the poorer eye.

Table 11 shows simple myopic astigmatism, minus cylinder at axis 90 in both eyes charted against acuity of stereopsis. Table 12 shows simple myopic astigmatism, minus cylinder at axis 180 in both eyes charted against acuity of stereopsis. It can be seen that increase of myopic cylinder error at axis 90 is accompanied with decrease in stereoptic acuity. However when the minus cylinder error was at axis 180, the acuity of stereopsis was maintained well as high as — 2.50 D.



The subjects themselves offered the explanation for this observation. When the cylinder inducing myopic astigmatism was at axis 90, they noted that the upper and lower margins of the dots appeared sharp and the lateral margins appeared blurred. On the other hand, when the myopic cylinder error was at axis 180, the lateral margins of the dots appeared clear, and the upper and lower margins were blurred. Therefore, in the first position the subjects could not see accurately the separations of the dots. On the other hand, when the cylinder error was

TABLE 13—*Induced Hypermetropic Anisometropia Versus Acuity of Stereopsis*

| Anisometropia, D | Acuity of Stereopsis |       |       |       |       | Circles |
|------------------|----------------------|-------|-------|-------|-------|---------|
|                  | 20/20                | 20/30 | 20/40 | 20/50 | 20/60 |         |
| 4 00             |                      |       |       |       |       | 2       |
| 3 50             |                      |       |       |       |       | 1       |
| 3 00             |                      |       | 1     |       | 8     | 4       |
| 2 50             |                      | 1     | 2     | 2     | 3     | 1       |
| 2 00             | 1                    | 2     | 2     | 2     | 2     | 3       |
| 1 50             | 2                    | 6     | 1     | 2     | .     | 1       |
| 1 00             | 5                    | 5     | 2     | 1     |       |         |
| 0 50             | 9                    | 4     |       |       |       |         |

at axis 180, the lateral margins appeared sharp, and good stereoptic acuity, despite a high refractive error, was possible.

Table 13 shows hypermetropic anisometropia charted against acuity of stereopsis. The distribution of the readings shows that stereoptic acuity decreases with increase of hypermetropic anisometropia but that it is possible for certain subjects to maintain good stereopsis despite

TABLE 14—*Cylinder Strength Versus Acuity of Stereopsis for Subjects with Induced Simple Hypermetropic Astigmatism, Cylinder Error at Axis 90*

| Cylinder Strength, D | Acuity of Stereopsis |       |       |       |       | Circles |
|----------------------|----------------------|-------|-------|-------|-------|---------|
|                      | 20/20                | 20/30 | 20/40 | 20/50 | 20/60 |         |
| 3 00                 |                      |       | 1     | 3     |       | 1       |
| 2 50                 |                      | 4     | 1     | 1     | 1     | 3       |
| 2 00                 |                      | 5     | 6     | 2     | 1     | 2       |
| 1 50                 | 1                    | 8     | 7     |       |       | 3       |
| 1 00                 | 1                    | 9     | 4     |       |       |         |
| 0 50                 | 7                    | 5     |       |       |       |         |
| 0 00                 | 11                   | 1     |       |       |       |         |

high induced anisometropia. Apparently, in fifteen seconds a practiced subject can gain sufficient visual information by means of varying his accommodation to obtain good stereopsis. As the anisometropia is increased, this becomes more and more difficult, and stereoptic acuity finally falls off.

Tables 14, 15 and 16 show hypermetropic cylinder errors at axis 90 in both eyes, at axis 180 in both eyes and at axis 90 in one eye and at axis 180 in the other respectively, charted against acuity of stereopsis.

All three tables show that with increased cylinder error, acuity of stereopsis falls off, the greatest decrease being with cylinders at crossed axes and less with cylinders at axis 90 and at axis 180. However, a noticeable feature of all three tables is the degree to which good stereopsis can be maintained despite high refractive error. The same interpretation might be put on this as in the situation of anisometropia—certain sub-

TABLE 15—*Cylinder Strength Versus Acuity of Stereopsis for Subjects with Induced Simple Hypermetropic Astigmatism, Cylinder Error at Axis 180*

| Cylinder Strength, D | Acuity of Stereopsis |       |       |       |       | Circles |
|----------------------|----------------------|-------|-------|-------|-------|---------|
|                      | 20/20                | 20/30 | 20/40 | 20/50 | 20/60 |         |
| 3.00                 |                      | 5     |       |       |       |         |
| 2.50                 |                      | 6     | 1     | 1     |       | 2       |
| 2.00                 |                      | 8     | 2     | 3     | 2     | 1       |
| 1.50                 | 2                    | 8     | 7     |       | 5     |         |
| 1.00                 | 1                    | 10    | 3     | .     |       |         |
| 0.50                 | 7                    | 5     |       |       |       |         |
| 0.00                 | 11                   |       |       |       |       |         |

TABLE 16—*Cylinder Strength Versus Acuity of Stereopsis in Subjects with Simple Hypermetropic Astigmatism Induced with Cylinder at Axes Crossed*

| Cylinder Strength, D | Acuity of Stereopsis |       |       |       |       | Circles |
|----------------------|----------------------|-------|-------|-------|-------|---------|
|                      | 20/20                | 20/30 | 20/40 | 20/50 | 20/60 |         |
| 3.00                 | .                    | 3     | 1     | 1     |       |         |
| 2.50                 |                      | 4     | 2     |       | 1     | 1       |
| 2.00                 | 2                    | 4     | 1     | 1     | 4     | 4       |
| 1.50                 | 1                    | 8     | 2     | 4     | 2     | 3       |
| 1.00                 |                      | 6     | 4     | 4     |       |         |
| 0.50                 | 1                    | 9     | 1     | 1     |       |         |
| 0.00                 | 15                   | 1     |       | .     |       |         |

TABLE 17—*Visual Acuity Versus Acuity of Stereopsis for Subject with Induced Simple Hypermetropic Astigmatism, Cylinder Error at Axis 90*

| Visual Acuity | Acuity of Stereopsis |       |       |       |       | Circles |
|---------------|----------------------|-------|-------|-------|-------|---------|
|               | 20/20                | 20/30 | 20/40 | 20/50 | 20/60 |         |
| 20/80         |                      |       |       |       | .     | 3       |
| 20/60         |                      |       | 1     | 4     | 1     | 4       |
| 20/40         | .                    | 4     | 14    | 1     | 1     | 2       |
| 20/30         | 1                    | 10    | 5     | 2     |       |         |
| 20/20         | 8                    | 18    |       |       |       |         |

jects can vary their accommodation sufficiently in fifteen seconds to maintain good stereoptic acuity.

Such an assumption seems confirmed when visual acuity is charted against acuity of stereopsis for induced hypermetropic cylinder errors, as shown in tables 17 and 18. The "scatter" in tables 14 and 15 is now eliminated, and a direct relationship of visual acuity to acuity of stere-

opsis becomes apparent. Therefore, in the case of hypermetropic cylinder error the ability to attain good stereoptic acuity accompanies the ability to attain good visual acuity.

TABLE 18—*Visual Acuity Versus Acuity of Stereopsis for Subject with Induced Hypermetropic Astigmatism, Cylinder Error at Axis 180*

| Visual Acuity | Acuity of Stereopsis |       |       |       |       | Circles |
|---------------|----------------------|-------|-------|-------|-------|---------|
|               | 20/20                | 20/30 | 20/40 | 20/50 | 20/60 |         |
| 20/80         |                      |       |       |       |       | 1       |
| 20/60         |                      |       | 2     | 1     | 5     | 1       |
| 20/40         |                      | 7     | 6     | 3     |       | 1       |
| 20/30         | 2                    | 18    | 6     |       |       |         |
| 20/20         | 7                    | 15    |       |       |       |         |

### III EFFECT OF CHANGING SIZE AND SEPARATION OF DOTS IN TARGET

The third part of this work is a study of the effect of varying the sizes and the separations of the dots in the targets. The procedures were similar.

TABLE 19—*Visual Acuity Versus Acuity of Stereopsis for Subjects with Induced Myopia in Both Eyes, Tested with Medium Separation of Dots*

| Visual Acuity | Acuity of Stereopsis |       |       |       |       | Circles |
|---------------|----------------------|-------|-------|-------|-------|---------|
|               | 20/20                | 20/30 | 20/40 | 20/50 | 20/60 |         |
| 20/160        |                      |       |       |       |       | 6       |
| 20/120        |                      | 2     | 4     | 1     | 5     | 4       |
| 20/80         | 2                    | 5     | 1     | 1     | 4     |         |
| 20/60         | 5                    | 1     | 4     |       | 1     | 2       |
| 20/40         | 6                    | 3     | 4     |       | 1     |         |
| 20/30         | 5                    | 8     |       | 1     |       |         |
| 20/20         | 20                   | 2     | 1     |       | 1     |         |
| Average       |                      | 20/32 | 20/40 | 20/77 | 20/86 |         |

TABLE 20—*Visual Acuity Versus Acuity of Stereopsis for Subjects with Induced Myopia in Both Eyes Tested with Wide Separation of Dots*

| Visual Acuity | Acuity of Stereopsis |       |       |       |       | Circles |
|---------------|----------------------|-------|-------|-------|-------|---------|
|               | 20/20                | 20/30 | 20/40 | 20/50 | 20/60 |         |
| 20/160        |                      |       |       |       |       | 6       |
| 20/120        |                      | 1     | 2     | 1     | 5     | 5       |
| 20/80         | 1                    | 2     | 2     | 3     | 2     | 2       |
| 20/60         | 2                    | 5     | 1     | 5     |       | 3       |
| 20/40         | 3                    | 3     | 5     | 3     | 2     |         |
| 20/30         | 2                    | 8     | 1     |       |       |         |
| 20/20         | 20                   | 5     | 1     |       | 1     |         |
| Average       |                      | 20/44 | 20/65 | 20/66 | 20/77 |         |

to the methods described in part II. The stereoptic acuity for the various sizes and separations of the dots was tested at different levels of visual acuity by inducing myopia in both eyes. A summary of the various slides used has previously been given.

*Observations*—Tables 19 and 20 show visual acuity charted against acuity of stereopsis for the two separations of dots. Increasing the separation from 50 to 75 minutes caused a very small decrease in acuity of stereopsis for all levels of visual acuity.

Tables 21, 22, and 23 show the amount of myopia charted against the acuity of stereopsis for three sizes of dots. The distribution of the cases indicates that the larger the size of the dots, the greater is the

TABLE 21—*Myopic Error Versus Acuity of Stereopsis in Subjects with Myopia Induced in Both Eyes, When Tested with Small Dots*

| Myopia, D | Acuity of Stereopsis |       |       |       |       | Circles |
|-----------|----------------------|-------|-------|-------|-------|---------|
|           | 20/20                | 20/30 | 20/40 | 20/50 | 20/60 |         |
| 3 00      |                      |       |       |       |       | 1       |
| 2 50      |                      |       |       |       |       | 9       |
| 2 00      |                      |       |       |       | 2     | 12      |
| 1 50      |                      |       | 1     |       | 12    |         |
| 1 00      |                      |       | 7     | 14    | 3     |         |
| 0 50      | 2                    | 6     | 16    | 1     |       |         |
| 0 00      | 17                   | 9     |       |       |       |         |
| Average   |                      | 0 20  | 0 69  | 0 97  | 1 46  |         |

TABLE 22—*Myopic Error Versus Acuity of Stereopsis for Subjects with Induced Myopia in Both Eyes, When Tested with Medium-sized Dots*

| Myopia, D | Acuity of Stereopsis |       |       |       |       | Circles |
|-----------|----------------------|-------|-------|-------|-------|---------|
|           | 20/20                | 20/30 | 20/40 | 20/50 | 20/60 |         |
| 3 00      |                      |       |       |       |       | 5       |
| 2 50      |                      |       | 2     | 2     | 2     | 5       |
| 2 00      | 1                    | 1     | 4     | 5     | 7     |         |
| 1 50      | 4                    | 5     | 5     | 8     | 3     |         |
| 1 00      | 12                   | 7     | 6     |       |       |         |
| 0 50      | 17                   | 8     |       |       |       |         |
| 0 00      | 26                   |       |       |       |       |         |
| Average   |                      | 0 98  | 1 56  | 1 80  | 1 96  |         |

TABLE 23—*Myopic Error Versus Acuity of Stereopsis for Subjects with Induced Myopia in Both Eyes, When Tested with Large Dots*

| Myopia, D | Acuity of Stereopsis |       |       |       |       | Circles |
|-----------|----------------------|-------|-------|-------|-------|---------|
|           | 20/20                | 20/30 | 20/40 | 20/50 | 20/60 |         |
| 3 00      |                      |       |       |       |       | 1       |
| 2 50      |                      | 1     | 3     | 3     | 1     | 2       |
| 2 00      |                      | 3     | 10    | 4     | 4     |         |
| 1 50      | 3                    | 8     | 7     | 1     | 3     |         |
| 1 00      | 9                    | 7     |       |       |       |         |
| 0 50      | 15                   | 1     |       |       |       |         |
| 0 00      | 24                   |       |       |       |       |         |
| Average   | 25                   | 1 40  | 1 90  | 2 12  | 2 38  |         |

amount of myopia necessary to reduce stereoptic acuity. If stereoptic acuity of better than 20/20 had been tested, it is presumed that much better than 20/20 acuity would be possible with the larger dots.

#### COMMENT

Now that the results in the three parts of the investigation have been presented, it is possible to evaluate them as a whole and to interpret the observations in one section of the study in the light of those in another section.

*Visual Acuity and Stereopsis*—The various results show a close correlation between visual acuity and stereoptic acuity. Defective visual acuity was the major factor which limited stereoptic acuity in the original series of clinical cases. When the values for patients showing suppression, learning tendency, hypermetropic anisometropia, hypermetropia of over  $+2.50$  D sphere equivalent and hypermetropia cylinder errors at crossed axes were removed from the graph, the relationship between the two acuities became obvious. In part II that relationship was again clearly defined when myopia in both eyes or in one eye, simple myopic astigmatism at axis 90 or simple hypermetropic astigmatism was induced. Stereoptic acuity tended to be fairly well maintained in the presence of induced simple myopic astigmatism, cylinder at axis 180. This was due to the subject's ability to focus on the vertical borders of the dots. In part III the relationship between the two acuities was reaffirmed, using larger dots and wider separations of the dots. These results all indicate that stereoptic acuity is directly dependent on visual acuity except with myopic cylinder error at axis 180.

*Causes Other Than Visual Acuity for Decreased Stereoptic Acuity*—The graph, presenting results for the 246 clinical subjects studied, includes values for patients showing suppression, hypermetropic anisometropia over  $+0.75$  D sphere equivalent, hypermetropic cylinder errors over  $+0.75$  D at axes more crossed than 45 degrees, the "learning" tendency and hypermetropia of over  $+2.50$  D sphere equivalent, all designated by special symbols. These patients will now be discussed, in the order indicated.

The subjects with suppression, with 2 exceptions, never showed an acuity of stereopsis greater than the amount of the suppression. Patients without fusion had no stereoptic acuity and were not included in the series. The quantitative testing of suppression by means of the Snellen chart, with letters missing, turned out to be very satisfactory. The subjects were found to suppress within the range of the size of letters shown on this chart. The fact that the test predicted decrease in stereoptic acuity seemed to confirm its value. Finally, the letters in the Snellen charts were already graded as to size, so that it was simple and convenient to grade suppression accordingly.

Patients with hypermetropic anisometropia were designated with a special symbol in the graph. In the second part of the study it was shown that hypermetropic anisometropia caused a lowering of stereoptic acuity but that certain persons could overcome a considerable error and still maintain good stereopsis. Apparently, the subjects accommodated alternately for the two slides and were able to obtain a good estimation of the separation of the dots, and therefore of their relative depth. Such results might not have been recorded if less than fifteen seconds had been allowed for the judgments. Two of the subjects who took these

tests were highly skilled at using their eyes. At first, the anisometropia caused a moderate loss of stereoptic acuity, but with practice the scores quickly improved. Therefore when anisometropia is induced, stereoptic acuity seems dependent on the subject's ability to use his eyes, his interest and attentiveness, the amount of previous practice and the amount of time he is given for his judgments, as well as on the amount of refractive error.

In part II, hypermetropic cylinder errors at crossed axes were found to cause a greater decrease of stereoptic acuity than did cylinder errors at parallel axes. It has already been noted that the amount of scatter for hypermetropia, shown in tables 14, 15 and 16, is greater than that for myopia, as shown in table 9. This may have somewhat the same significance as the results for induced anisometropia. Hypermetropic cylinder errors at crossed axes tend to reduce stereoptic acuity, but the error may be overcome and good stereoptic acuity obtained if the subject's interest, attention and facility at using his accommodation are at a high level.

The importance both of the learning of stereopsis and of the learning factor in this particular test can now be assessed. First, it was noted in part I that the learning factor was present in the sample of the population represented and that subjects showing this tendency formed a large proportion of patients who did not gain a stereoptic acuity commensurate with their visual acuity. Second, comparison of tables 1 and 9 shows that the average visual acuities for each level of stereopsis are lower in table 1. The patients in table 1 were all taking the test for the first time, while the subjects in table 9 were trained observers. The difference in the averages in the two tables seems to be due to our inability in the first tests (table 1) to eliminate all subjects with lowered acuity of stereopsis due to causes other than lowered visual acuity, to the learning factor of the subjects and to the learning factor in the test itself. The test's learning factor, so revealed, appears to be small and unimportant. Third, review of tables 9, 21, 22 and 23 shows that when simple myopia is induced in both eyes acuity of stereopsis falls off as visual acuity decreases. These results were obtained by repeated testing on different days. Therefore, if a great learning factor was present, there would be a great scatter of the results in the tables. No such scatter is present, indicating that learning in cases of simple myopia, following the original session, is insignificant. The same analysis would apply to the results in table 10, for subjects with induced simple myopia in one eye. The scatter in this table is still small but greater than that for simple myopia in both eyes. During the testing of subjects with induced myopia in one eye variations in visual acuity occurred.

This was apparently due to variations in the relaxation of accommodation. Therefore the scatter in table 10 is probably due to such variations rather than to learning. On the other hand, subjects with anisometropia and hypermetropic astigmatism do show improvement in stereoptic vision with practice, and the scatter in tables 13, 14, 15 and 16 seems to be due partly to this learning factor. To sum up, subjects can be taught to gain their full stereoptic acuity in one or two sessions. After that learning is insignificant, except possibly in cases in which a great deal of anisometropia or hypermetropic astigmatism must be overcome.

In part I hypermetropia was not found to be any bar to good stereoptic acuity. However, several of the subjects with high hypermetropia noted difficulty in maintaining the small dots in clear vision. Attempts to formulate an experiment to fit into part II of the study were not helpful. The subjects tended to accept a minus sphere up to a certain level with no loss of stereopsis. Beyond that, vision suddenly became blurred, and stereoptic readings were not possible. Thorne<sup>3</sup> mentioned that hypermetropia causes decrease in acuity of depth perception, but no direct evidence for this statement has been found here.

*Muscle Balance and Stereopsis*—It can be seen from tables 6, 7 and 8 that there is no correlation of Maddox rod readings for near and distant vision, convergence and acuity of stereopsis. Apparently, stereopsis as tested here has no relationship to minor heterophorias or to decrease in power of convergence. This is at variance with the observations of Howard.<sup>1</sup> However, suppression was found to reduce stereoptic acuity, and lack of fusion was a complete bar to stereopsis. Only when suppression accompanies heterophorias can decrease of stereopsis be expected.

*Size of Test Objects and Stereopsis*—It has been noted that increased size of the dots allowed increased acuity of stereopsis. Samsonowa<sup>4</sup> found that acuity of stereopsis is related to the length of the vertical borders of the objects viewed, and not to the area of the objects or the length of the horizontal borders. Anderson and Weymouth,<sup>5</sup> testing depth perception by means of vertical strings, noted that when the length of the string was increased up to the diameter of the macula depth perception improved, but beyond that no improvement was

3 Thorne, F. H. *Ophthalmology in Aviation*, Arch. Ophth., **19** 253-277 (Feb.) 1938.

4 Samsonowa, V. G. Einfluss der Objektform auf das stereoskopische Sehen, Arch. f. Ophth. **135** 30-48, 1936.

5 Anderson, E. E., and Weymouth, F. W. Visual Perception and the Retinal Mosaic, Am. J. Physiol. **64** 561-691, 1923.

obtained. In the present work the improvement in stereopsis with increased size of the dots is probably due to the increased vertical border.

*Separation of Test Objects and Stereopsis*—In this investigation a small decrease in acuity of stereopsis occurred when the separations were increased from 50 to 75 minutes. Langlands<sup>6</sup> noted a decrease in depth perception as separation was increased. The same author, using eccentric fixation, found that when the angle from the macula increased visual acuity declined at the same rate as did stereoptic acuity. Frubose and Jaensch<sup>7</sup> noted a steady decrease in acuity of depth perception as separations were increased to 6 degrees, and a still greater decrease beyond that. The present investigation would confirm that in the region of the macula increased separation of the test objects reduces acuity of stereopsis for all levels of visual acuity.

#### SUMMARY AND CONCLUSION

A new series of slides for the quantitative testing of acuity of stereopsis is described.

A method for obtaining a quantitative estimation of the degree of suppression is discussed.

A series of clinical cases was studied and clinical experiments were carried out, using the test for stereoptic acuity. The following conclusions were drawn:

- 1 Stereoptic acuity as tested here varied directly as the visual acuity.
- 2 Decrease in stereoptic acuity accompanied increase in the amount of suppression.
- 3 Refractive errors affected stereoptic acuity as follows:
  - (a) Acuity of stereopsis was reduced in proportion as the error increased in subjects with (1) myopia in one eye, (2) myopia in both eyes, (3) myopic astigmatism, axis 90.
  - (b) Acuity of stereopsis was reduced but could be partially maintained by the subject's efforts in cases of (1) myopic astigmatism, axis 180, (2) hypermetropic astigmatism, axes 90 and 180 and crossed axes, (3) anisometropia.
  - (c) Acuity of stereopsis was not affected in subjects with hypermetropia.

<sup>6</sup> Langlands, N. M. Experiments on Binocular Vision, Great Britain Privy Council, Medical Research Council, Special Report Series, no. 1933, London, His Majesty's Stationery Office, 1929.

<sup>7</sup> Frubose, A., and Jaensch, P. A. Der Einfluss verschiedener Faktoren auf die Tiefenschärfe, *Ztschr. f. Biol.* 78:119-132, 1923.



4 An initial learning of stereoptic acuity occurs The test does not seem to have a significant learning factor

5 Increase in the size of the test objects improved stereoptic acuity  
Increase in the separation of the test objects decreased stereoptic acuity

6 Convergence, heterophorias, age and accommodation showed no correlation with acuity of stereopsis

The Director of Medical Services for Air gave permission to publish this article

# ALKALI BURNS OF THE EYE

## II Clinical and Pathologic Course

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THE PROGRESSIVE nature of severe alkali burns of the eyes and the frequency of secondary complications are well known. The purpose of this communication is to outline the distinctive clinical and pathologic features, which may yield clues to the mechanism of action, and to emphasize the secondary reactions, against which are directed many of the therapeutic measures

Except for minor differences in the rate of penetration and the intensity of opacification, the clinical courses of burns produced by a variety of alkalis, e g, lye, lime (calcium oxide) and ammonia, are remarkably similar<sup>1</sup> The alkalinity of the solution is probably the most important factor governing the severity of the lesion, and the rabbit cornea is damaged by solutions more alkaline than those with  $p_H$  of 11.5<sup>2</sup> The material for the present study included sodium hydroxide burns of the rabbit eye and clinical observations on several types of alkali burns in human eyes

### CLINICAL COURSE

#### MODERATELY SEVERE SODIUM HYDROXIDE BURN OF THE RABBIT EYE

Irrigation of one-half the rabbit cornea for three minutes with twentieth-normal (0.2 per cent) sodium hydroxide made isotonic by the addition of sodium chloride produced a moderately severe lesion, which eventually healed The accompanying series of photographs (figs. 1 to 3) follow the course of such a burn in a single rabbit eye

*During Irrigation*—The cornea gradually acquired an opalescent cloudiness of silky texture, and the adjacent sclera in contact with the alkali became translucent. The corneal epithelium adhered poorly to the underlying stroma and could be wiped off easily Gelatinous material accumulated in the conjunctival cul-de-sac.

From the Wilmer Ophthalmological Institute of the Johns Hopkins University and Hospital

1 Hughes, W F, Jr Alkali Burns of the Eye A Review of the Literature and Summary of Present Knowledge, Arch Ophth 35 423-449 (April) 1946

2 Friedenwald, J S, Hughes, W. F, Jr, and Herrmann, H Acid-Base Tolerance of the Eye, Arch Ophth 31 279-283 (April) 1944



Figure 1

(See legend on opposite page)

*Fifteen Minutes* (fig 1 A)—The cornea had become moderately cloudy and thickened as a result of edema. The adjacent limbus was ischemic, and the nearby blood vessels had segmented columns of blood, surrounded with petechial hemorrhages. Conjunctival edema developed. Examination of the anterior chamber with the slit lamp revealed an aqueous ray.

*Five Hours* (fig 1 B)—The corneal epithelium had desquamated, leaving an area which stained green with fluorescein. Conjunctival edema was more pronounced, and a small amount of mucous discharge had accumulated in the lower cul-de-sac.

*Three Days* (fig 1 C)—The conjunctival edema had largely subsided, but many deep hemorrhages persisted in the episcleral and scleral tissues above. The corneal edema had spread to the lower, or unburned, portion of the cornea. The iris was slightly congested and thickened.

*Ten Days* (fig 1 D)—The edema of the lower half of the cornea had disappeared, and the corneal opacification was less intense. Blood vessels began to encroach on the limbus about the fifth day, and after ten or twelve days superficial loops extended 2 to 3 mm into the cornea. The vessels sometimes exhibited irregular dilatations, with hemorrhages surrounding the bulbous ends. Vessels did not enter the corneal opacity from the ischemic area, but they arose from intact vessels around the edges of the corneal opacification. If the necrosis of limbal vessels was only superficial, vessels from deeper loops entered the posterior layers of the cornea in the form of straight, brushlike projections. The most intense vascularization of the cornea could be produced by the intracorneal injection of alkali immediately adjacent to, but not involving, the limbus. Small injections of alkali in the center of the cornea, leaving a rim of clear cornea around the entire periphery, produced little, or no vascularization. It was possible for vessels to pass through short stretches of relatively clear cornea if the lesion to which they were directed was sufficiently large.

*Seventeen Days* (fig 1 E)—The vascularization of the cornea was clearly visible to the left of the relatively thin opacity.

#### EXPLANATION OF PLATE

Fig 1—A, rabbit eye fifteen minutes after three minute irrigation of the upper half of the cornea with a solution of twentieth-normal (0.2 per cent) sodium hydroxide made isotonic by the addition of sodium chloride. This exposure has produced a dense white corneal opacification, with ischemia of the adjacent limbal region above. Figure 1 B to F and figure 2 A to C, inclusive, are photographs of the same eye at various intervals after exposure.

B, five hours after exposure. Moderate conjunctival edema has developed, the corneal epithelium has sloughed and shreds of desquamated tissue and exudate are present in the lower cul-de-sac.

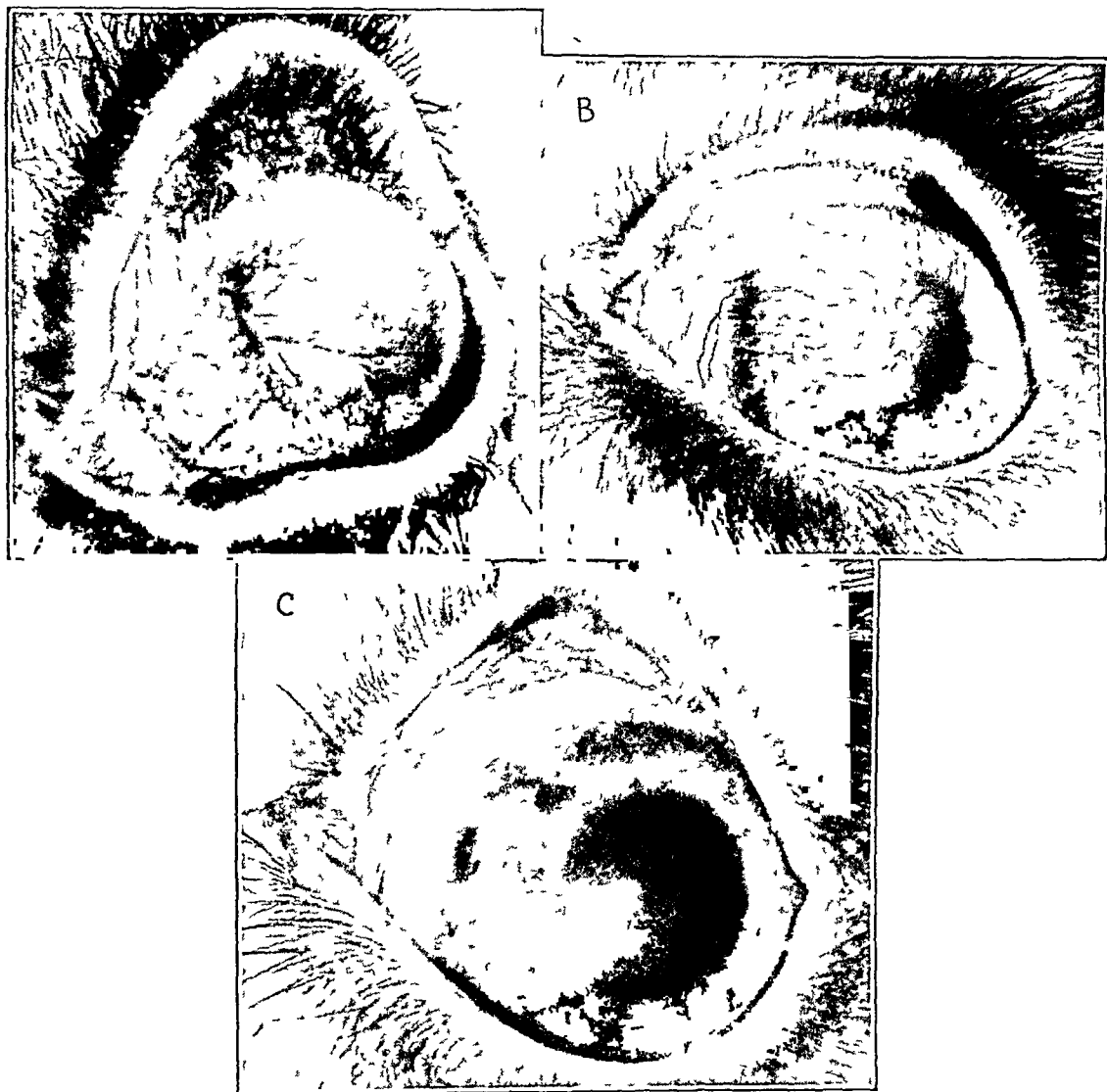
C, three days after exposure. The conjunctival edema has already subsided leaving subconjunctival hemorrhages in the necrotized tissue above. The corneal edema has spread from the original lesion to involve previously clear cornea.

D, at end of ten days. The secondary edema of the cornea, below, has entirely disappeared, and the opacification, above, is relatively light.

E, at end of seventeen days. Large, superficial vessels are proceeding into the burned area from the uninvolved limbal plexus laterally.

F, at end of twenty-seven days. The corneal infiltration has become heavier, and vessels can also be seen entering the area from the right side of the lesion above.

*Twenty-Seven Days (fig 1F)*—The opacity had become more dense because of a cellular infiltration in the cornea, and this was associated with increased conjunctival congestion and some mucopurulent discharge



**Fig 2—A**, eye forty-two days after exposure. Shallow ulceration of the cornea is present over the dense, yellowish white infiltration, and large vascular trunks with many branches have pushed into the lesion from three sides. In the vascularized area the mild haziness is largely contributed by the edema.

**B**, three months after exposure. The corneal opacification has cleared greatly, leaving some irregularity of the surface, mild edema and faintly visible blood vessels. An iridescent opacity of the lens capsule is limited to a small, round area in the center of the pupil and does not extend into the anterior cortex.

**C**, ten months after exposure. The corneal opacity is less intense, largely owing to disappearance of the corneal edema and vascularization. Regenerating corneal epithelium has carried limbal pigment onto the cornea at 11 o'clock, the so-called pigment slide. An elevated scar persists centrally. The haziness surrounding this is largely caused by the deposition of cholesterol. A few peripheral anterior synechias lie under the burned area, from 9 to 12 o'clock. Development of the capsular cataract has not progressed.

*Forty-Two Days* (fig 2A)—The corneal infiltration was somewhat more localized, and blood vessels were making their way into the area

*Ninety-Five Days* (fig 2B)—The area of dense corneal infiltration had disappeared, leaving the surface of the cornea in this region uneven. The vascularization, which was partially faded, arose from limbal blood vessels at the side of the ischemic area, at 11 o'clock, and entered the cornea in a single plane about one third of the thickness of the cornea beneath the surface. Mild edema of the corneal epithelium and stroma persisted in the central portion of the lesion, and the endothelium was cloudy. Several peripheral anterior synechiae underlay the most severely involved portion of the cornea. The anterior capsule of the lens had a sharply circumscribed opacity with a metallic sheen, but the underlying cortex of the lens remained clear.

*Next Seven Months*—During this time the cornea became clearer, largely because of disappearance of the corneal edema and fading of the vascularization.



Fig 3—Central corneal opacity shown in figure 2C, as seen with the slit lamp. A yellowish white opacity lies in the central third of the cornea, overlying which is a network of blood vessels, many of them bloodless. The underlying corneal endothelium is thickened. A vascularized scar, below, is elevated above the surface of the cornea. In the middle third of the stroma are many needle-like crystals of cholesterol.

into so-called ghost vessels, which contained no blood (fig 2C). Examination with the slit lamp at ten months (fig 3) revealed the presence of many needle-like crystals (probably cholesterol) deep within the corneal stroma.

#### MILD SODIUM HYDROXIDE BURN OF THE RABBIT EYE

Irrigation of the rabbit eye with twentieth-normal sodium hydroxide for thirty seconds or less without subsequent lavage produced a relatively mild lesion. As compared with that described in the preceding section, the acute conjunctival symptoms (e g, edema, necrosis of limbal vessels and petechial hemorrhages) were less pronounced, the corneal opacifica-

tion was less dense, ulceration rarely extended deeper than the epithelium, vascularization of the cornea was usually limited to a few loops of superficial vessels which faded within a week or two, late infiltrations of the cornea were unusual, and iritis was mild

#### SEVERE SODIUM HYDROXIDE BURN OF THE RABBIT EYE

Devastating lesions of the rabbit eye could be produced by irrigation of the entire cornea of a proptosed eye for over three minutes with a twentieth-normal solution of sodium hydroxide. Noteworthy in the clinical course of such burns were necrosis of the conjunctiva, with desquamation of large sheets of tissue, pearly white, ischemic necrosis of the limbal blood vessels, accompanied with hemorrhages, almost complete opacification of the cornea, with early desquamation of the epithelium, poor staining of the opaque cornea with fluorescein in spite of the fact that the surface was completely denuded of epithelium, purulent infiltration of the cornea within a week or ten days, associated with deep ulceration and perforation, extreme congestion and thickening of the iris (thrown into folds), frequently associated with hypopyon, and a capsular cataract, visible after a few hours. Descemet's membrane was remarkably resistant to alkali, often remaining clear and intact although the overlying cornea became opaque and sloughed. In spite of the obvious necrosis of the conjunctiva and the purulent nature of the reaction, symblepharon practically never ensued in the rabbit. The necrosis of the limbal vessels was ordinarily so complete that superficial vascularization did not occur, although deeper vessels might arise from less severely burned portions of the limbus. The regenerating conjunctiva might encroach on the ulcerated cornea, but fleshy, pterygium-like growths over the center of the cornea did not ordinarily occur in rabbits.

#### SPECIAL CHARACTERISTICS OF ALKALI BURNS OF THE HUMAN EYE

Alkali burns of the human eye have a strong predisposition to development of localized corneal infiltrations about one to three weeks after injury.

In figure 4*A* is pictured a mild lye burn four hours after injury. Little cloudiness of the cornea was detectable at this time. However, eight days later (fig 4*B*) a localized, round area of corneal infiltration had developed at 8 o'clock, toward which was directed a sheaf of blood vessels from the limbus. The overlying corneal epithelium took a faint green stain with fluorescein. Similar late infiltrations occurred in rabbit eyes burned with sodium hydroxide (fig 4*C*).

Ischemic necrosis of the limbal region notoriously carries an unfavorable prognosis. Vascularized connective tissue frequently arises from the necrotic area and proceeds like a pterygium over the surface of

the burned cornea (fig 5 *A* and *B*) This fleshy membrane may also be continuous with adhesions between the lids and the globe, producing a complete symblepharon (fig 5 *C*) The direct relation between ischemic necrosis of the limbus and the tendency to late infiltration and ulceration of the cornea is less certain

Severe corneal burns in human eyes are prone to undergo relapses, in which the eye becomes irritable and small ulcerations and low grade iritis appear The cornea may become progressively thinner, frequently resulting in staphyloma if there is an associated secondary glaucoma

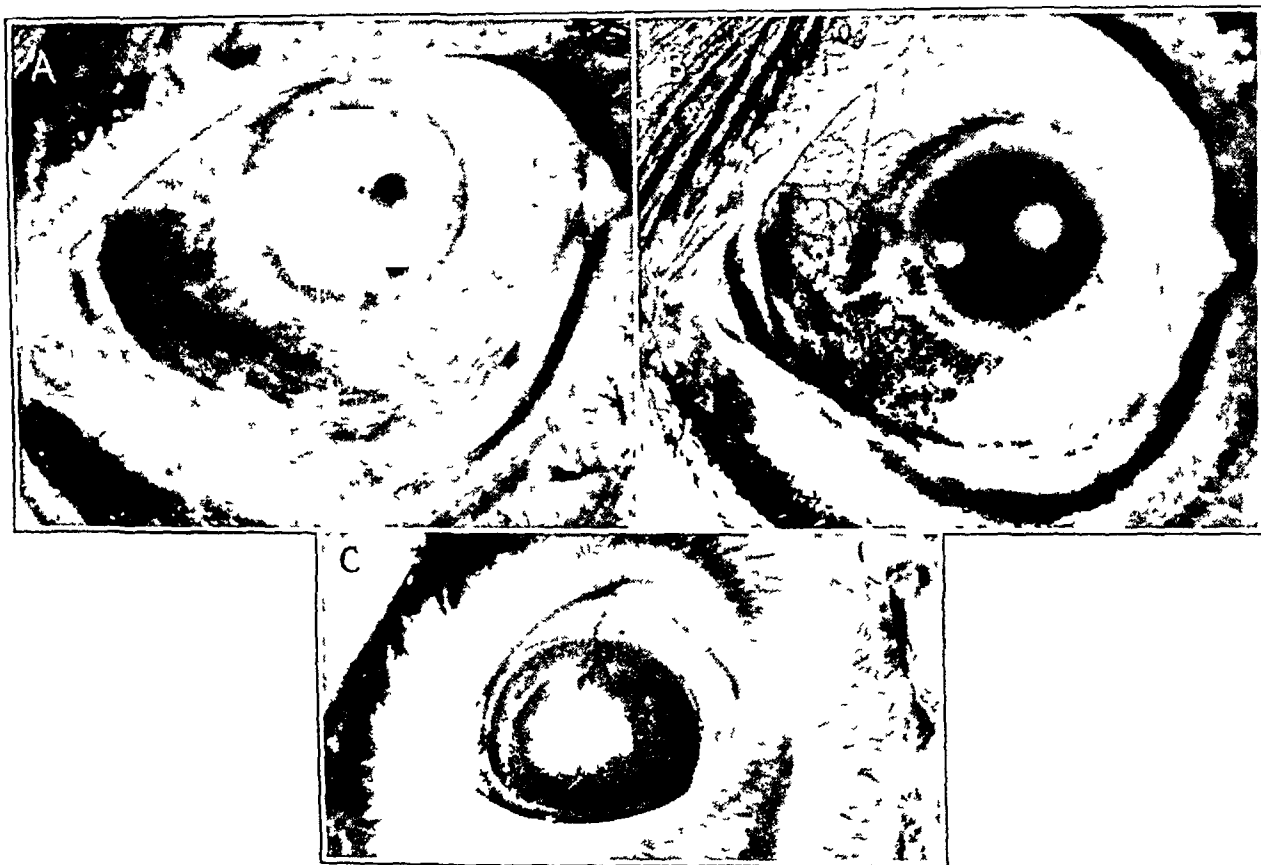


Fig 4—*A*, lye burn of a human eye four hours after injury Some mucus lies on the limbus at 5 o'clock, but there is only a suggestion of corneal haziness at 8 o'clock.

*B*, same eye as that shown in *A* eight days after injury A localized, round area of corneal infiltration has developed, toward which limbal blood vessels are directed

*C*, corneal infiltration, which did not appear until five days after injection of 0.1 cc of hundredth-normal sodium hydroxide into the cornea of a rabbit eye

#### STAGES OF CLINICAL COURSE OF ALKALI BURNS

A review of the clinical course shows that the changes fall naturally into three stages (1) an acute stage consisting of ischemic necrosis and edema of the conjunctiva, sloughing of the corneal epithelium, opacification and edema of the substantia propria of the cornea and iritis (2) a stage of reparation including the subsidence of conjunctival



and corneal edema, regeneration of the epithelium, vascularization of the cornea with slow clearing of the opacification and disappearance of the iritis, and (3) a stage of late complications, which may include symblepharon and overgrowth of the cornea with a vascularized membrane, late corneal infiltrations, persistent or recurrent corneal ulceration, permanent corneal opacification, staphyloma of the cornea, persistent or exudative iritis, secondary glaucoma and cataract

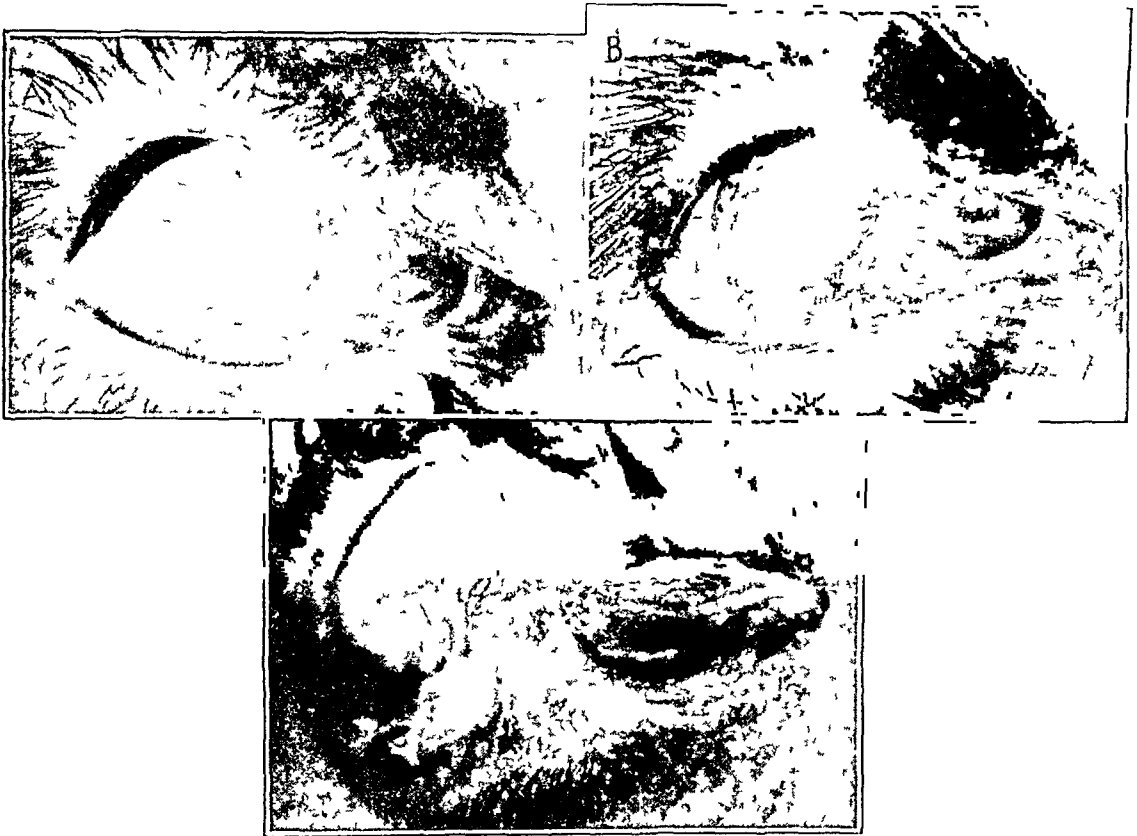


Fig 5—*A*, severe burn of a human eye with lime a few hours after injury, illustrating the extreme ischemic necrosis of the limbal region, in an area from 3 to 6 o'clock

*B*, later photograph of the eye shown in *A*. A tongue of vascularized connective tissue is growing over the damaged cornea from the region of ischemic necrosis

*C*, complete symblepharon, present months after a severe burn with lime

#### PATHOLOGIC COURSE

The histologic changes in sodium hydroxide burns of the rabbit eye will be described according to the stages of reaction just outlined, in an effort to elucidate some of the clinical features. There are several acute processes directly attributable to the necrotizing action of the alkali and secondary reactions, which are reparative in nature or result in secondary complications

## ACUTE STAGE

*Histologic Evidence of Rate and Depth of Penetration of Alkali*—In the moderately severe alkali burn previously described (irrigation of the rabbit eye for three minutes with twentieth-normal sodium hydroxide), the corneal endothelium showed signs of disintegration in the burned area three minutes after the irrigation was completed. At the end of ten minutes (fig 6) the endothelium underlying the exposed area had largely been desquamated. The alkali apparently penetrated the posterior chamber of the eye and altered the permeability of the vessels in the ciliary processes, resulting in edema of the ciliary processes within an hour (fig 7A) and sometimes a large cystic bleb, similar to that described by Greef (fig 7B). The capsule of the lens was damaged early, particularly within the pupillary space, and in twenty-four hours a capsular opacification could be detected clinically.

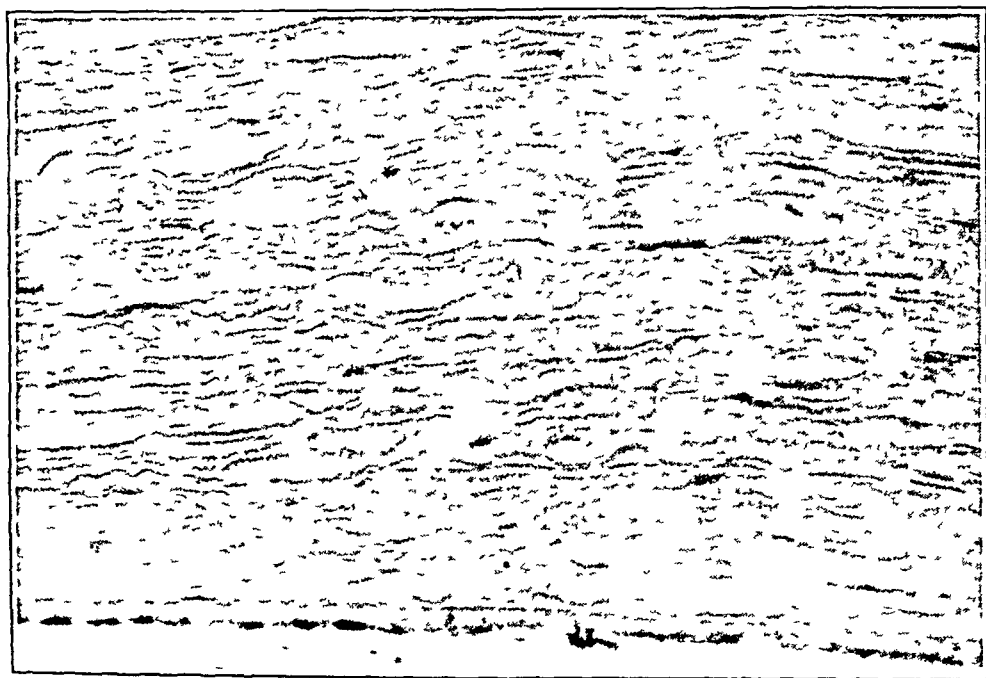


Fig 6—Section of the posterior layers of the rabbit cornea ten minutes after three minute irrigation with twentieth-normal sodium hydroxide. In the burned area, on the right, the endothelium has already become fragmented and has partially desquamated.

Unless otherwise noted, subsequent histologic material was prepared by irrigation of one-half the proptosed rabbit eye for three minutes with isotonic twentieth-normal sodium hydroxide and fixation in Zenker's fluid, and the sections were stained with hematoxylin and eosin.

*Conjunctival Changes*—At the end of three minutes (fig 8A), the conjunctival epithelium had been entirely sloughed, and the subconjunctival tissue was disorganized. The cellular structure of the walls of blood vessels was disintegrated, and basophilic shadows of red blood cells remained in the lumens. At the end of thirty minutes the burned conjunctiva had completely lost its normal structure. At one hour swirls of eosinophilic, amorphous material (probably serous exudation) were present, and at the end of two hours polymorphonuclear cells appeared.

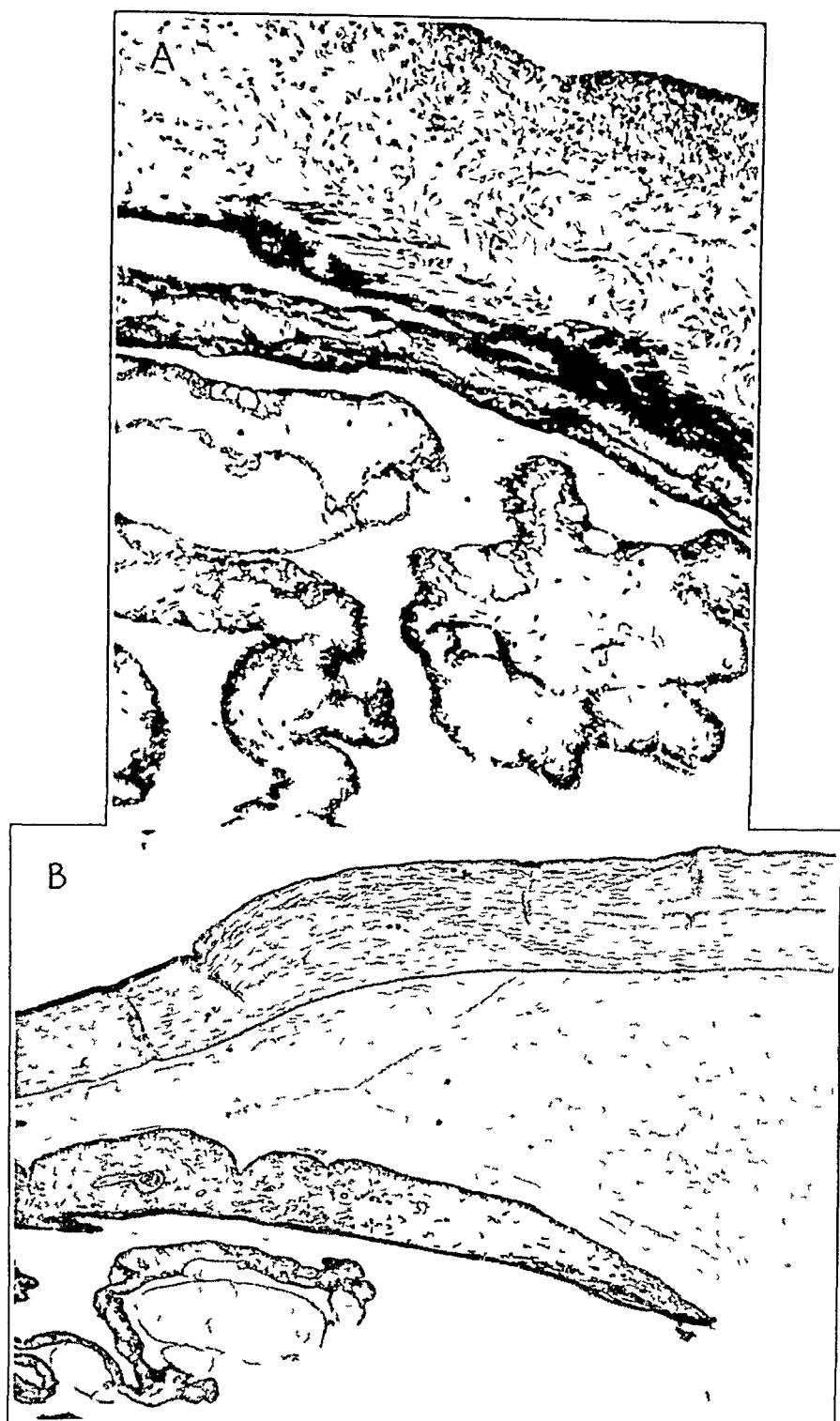


Fig 7—A, ninety minutes after exposure Edema of the ciliary processes  
 × 130

B, forty-five minutes after exposure A large cystic bleb has developed in  
 the ciliary processes ("Greef cyst") × 35

*Necrosis of Blood Vessels at the Limbus*—As noted in the section at the end of three minutes (fig 8A), the endothelial lining of the limbal blood vessels showed signs of disintegration. After thirty minutes (fig 8B) the wall of the

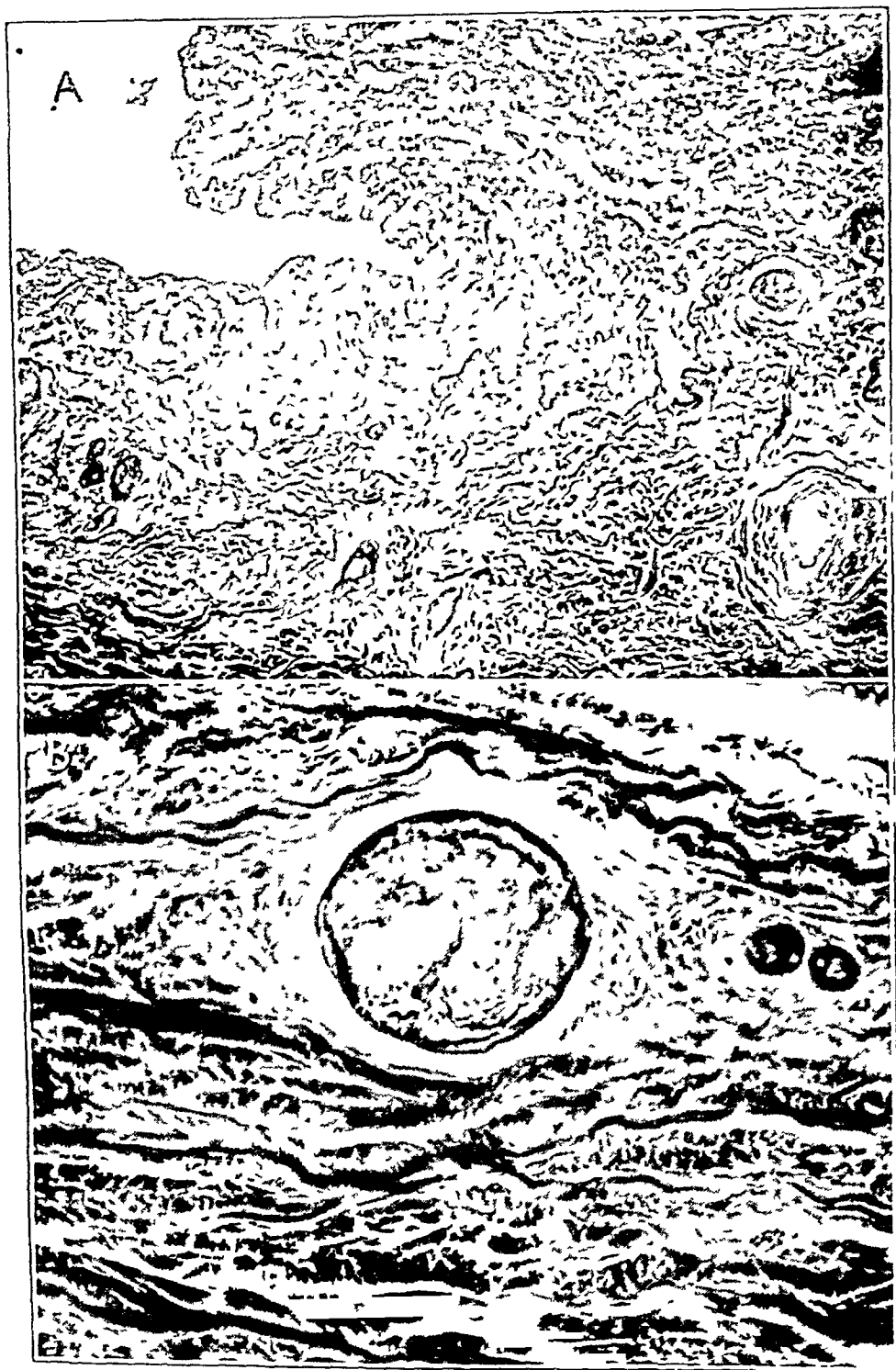


Fig 8—A, three minutes after irrigation with twentieth-normal sodium hydroxide was stopped. There are complete desquamation of the conjunctival epithelium and extensive necrosis of all the deeper structures  $\times 300$

B, section through the superficial scleral tissue of the limbus thirty minutes after exposure. The blood vessel has become an acellular rim surrounding a thrombus  $\times 670$

vessel became an acellular rim surrounding a thrombus. The underlying sclera was characterized by feathery lamellations and small bundles, representing cross sections of remaining fibers.

*Early Corneal Changes*—The corneal epithelium became peglike, with displacement of the cell nuclei toward the surface (fig 9 A). The cornea was

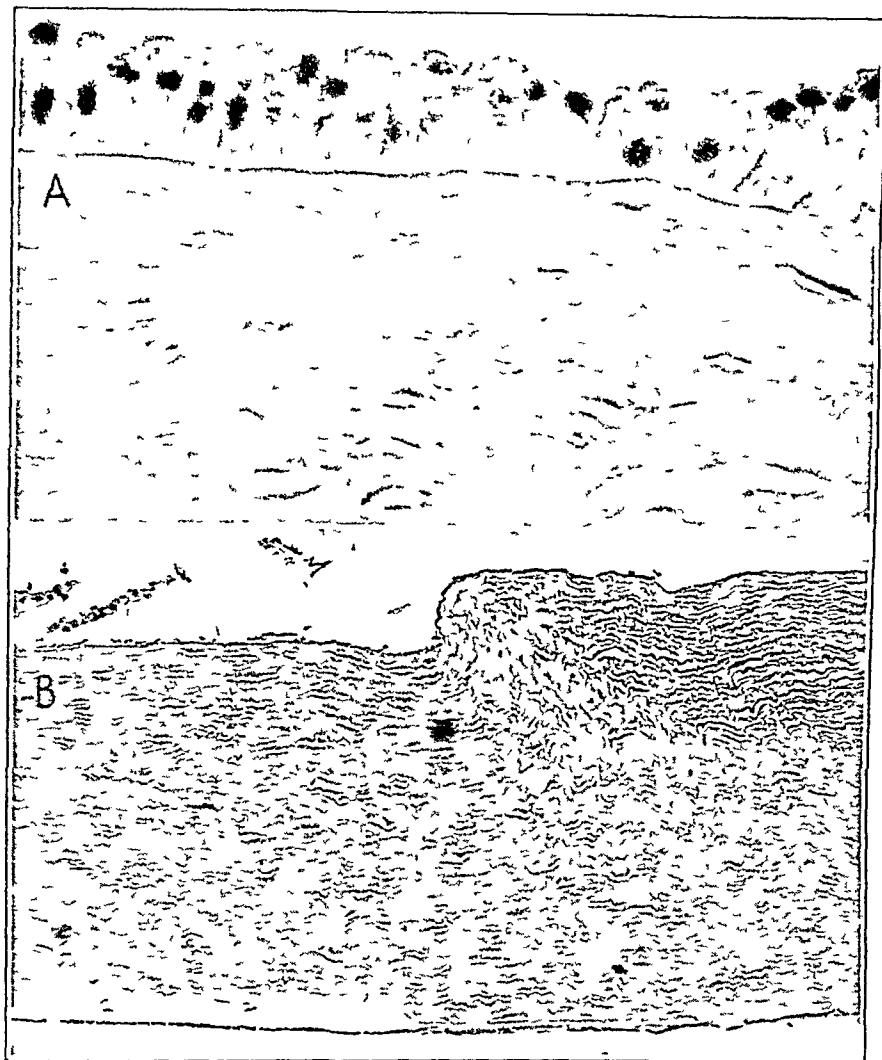


Fig 9—*A*, section of corneal epithelium three minutes after exposure. The more severely burned portions on the right show anterior displacement of the cell nuclei, peg-shaped cells and beginning detachment of the epithelium from the underlying stroma  $\times 480$ .

*B*, from the same eye as that pictured in *A*, showing fragments of partially desquamated epithelium on the left, and, on the right, complete denudation of epithelium  $\times 130$ .

rapidly denuded of epithelium because the basal layers became loosened from the underlying stroma and the cell membranes and cytoplasm disintegrated (fig 9 *A* and *B*).

After irrigation with sodium hydroxide, the corneal stroma appeared washed out (fig 10 *A*), leaving horizontal lamellas separated by feathery striations (fig 12 *A*). Metachromatic staining of intercellular mucoid (toluidine blue stains mucoid purplish) began to decrease after eight hours and almost disappeared twenty-four hours after exposure to alkali. Fragmentation and disappearance of the stroma cells were clearly visible at the end of three minutes (fig 10 *B*), and by eighteen hours the necrotized area had become acellular. The endothelium underlying the exposed area was rapidly destroyed by the alkali, and corneal edema developed (fig 10 *C*). As seen under high power magnification, the nuclei in edematous areas were stretched into angular shapes by the distorted fibers and membranes (fig 10 *D*). After two hours polymorphonuclear cells began to enter the cornea peripherally (fig 11 *A*) and were usually found in the loose textured, superficial layers of the cornea nearest the burned area (fig 11 *B*).

*Iris*—As soon as three minutes after irrigation with twentieth-normal sodium hydroxide traces of serum could be seen in the anterior chamber, and after thirty minutes to one hour (fig 12 *A*) the anterior chamber was filled with serous exudation. Within four hours a few polymorphonuclear cells could be found in the anterior chamber, and after four days they were present in great numbers in the anterior chamber and the iris (fig 12 *B*). The purulent reaction usually subsided within several days, but the iris continued to show increased vascularity, edematous thickening and early fibrosis. Disorganization of the pigment epithelium occurred later.

It has already been mentioned that the ciliary processes were affected soon after exposure to alkali, with development of edematous bullae of the surface epithelium (fig 7 *B*) and edema of the processes (fig 7 *A*). This acute process usually subsided after one week.

#### REPARATIVE STAGE

*Conjunctiva*—In the rabbit, the regeneration of the conjunctival epithelium was rapid. At the end of forty-eight hours the surface of the burned conjunctiva was covered with new epithelium, and this might continue growing over the surface of the adjacent burned cornea (fig 13 *A*). Astonishingly little fibrosis occurred in the damaged conjunctiva of the rabbit eye.

*Cornea*—Six hours after exposure to alkali a single layer of rounded epithelial cells was found overlying the burned stroma in the periphery (fig 13 *B*). These plump regenerating cells proceeded over acellular areas of burned stroma without difficulty and rapidly became stratified, with flattening of the superficial layers (fig 14). However, if the underlying stroma was unduly affected by purulent infiltration or rough areas of ulceration, the new-formed epithelium adhered poorly. In addition, excessive and irregular thickening of the epithelium might develop, the cells being of irregular sizes and shapes, with uneven stratification (figs 15 *A* and *B*).

Vascularization of the cornea proceeded in from the limbal vessels soon after seven days. Most often the vessels were located in the loose, damaged tissue of the anterior third of the stroma (fig 13 *A*), but they might lie deep within the cornea if the superficial limbal vessels had been thrombosed or the corneal burn was severe (fig 15 *B*).

Repair of the acellular zones in the burned stroma began after twenty-four hours with the appearance of elongated cells in the adjacent, less involved area.



Figure 10

(See legend on opposite page)

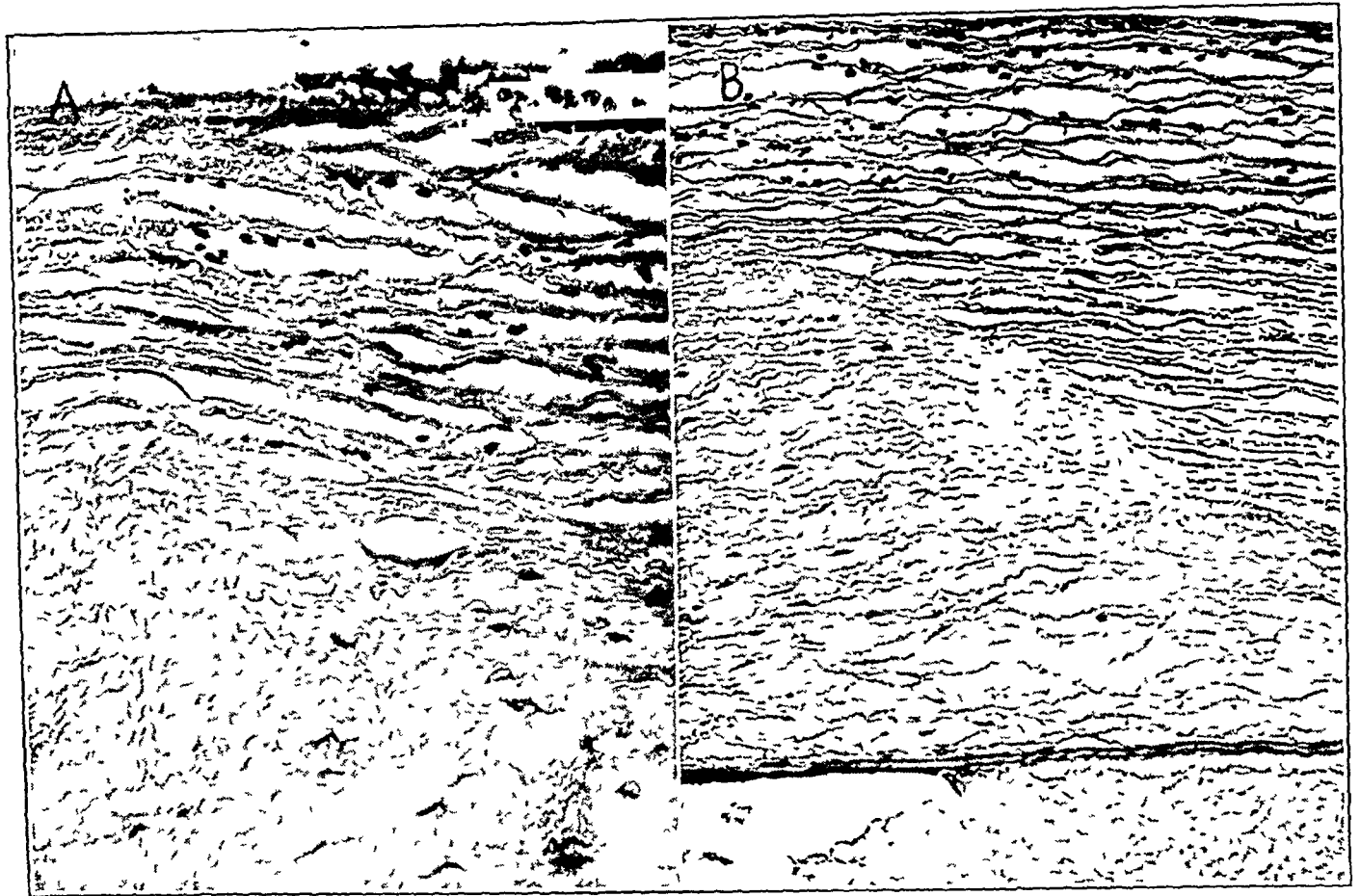


Fig 11—*A*, section at periphery of the rabbit cornea burned with twentieth-normal sodium hydroxide two hours previously. Polymorphonuclear cells have already begun to infiltrate into the anterior layers of the stroma.

*B*, section of rabbit cornea eight hours after exposure. The corneal epithelium has sloughed completely, polymorphonuclear cells have infiltrated into the loose-textured stroma anteriorly, dark-staining, elongated cells are present in the less severely burned stroma on the left, the endothelium has desquamated on the right, and exudation into the anterior chamber has already developed.

#### EXPLANATION OF PLATE

Fig 10—*A*, section of rabbit cornea ten minutes after ten minute irrigation with tenth-normal sodium hydroxide. The anterior third appears washed out, and metachromatic staining with toluidine blue in such areas revealed loss of mucoid. Mallory's connective tissue stain.

*B*, same eye as that from which sections appear in figure 9 *A* and *B*, showing contrast between the burned corneal stroma, above, and the normal stroma, below, to which the alkali apparently did not penetrate.  $\times 670$

*C*, same eye as that pictured in figure 5 *C*, forty-five minutes after exposure, showing edema of the corneal stroma in the area where both epithelium and endothelium have desquamated.

*D*, section of highly edematous cornea five days after the intracorneal injection of a solution of sodium carbonate of  $p_H$  9.0. Descemet's membrane was found detached under this area, with cellular proliferation and irregular regeneration of the corneal endothelium, probably the results of mechanical damage. Similar distortion of cell fibers and membranes is seen after exposure to solutions of higher  $p_H$ , which also damage the corneal endothelium.  $\times 670$



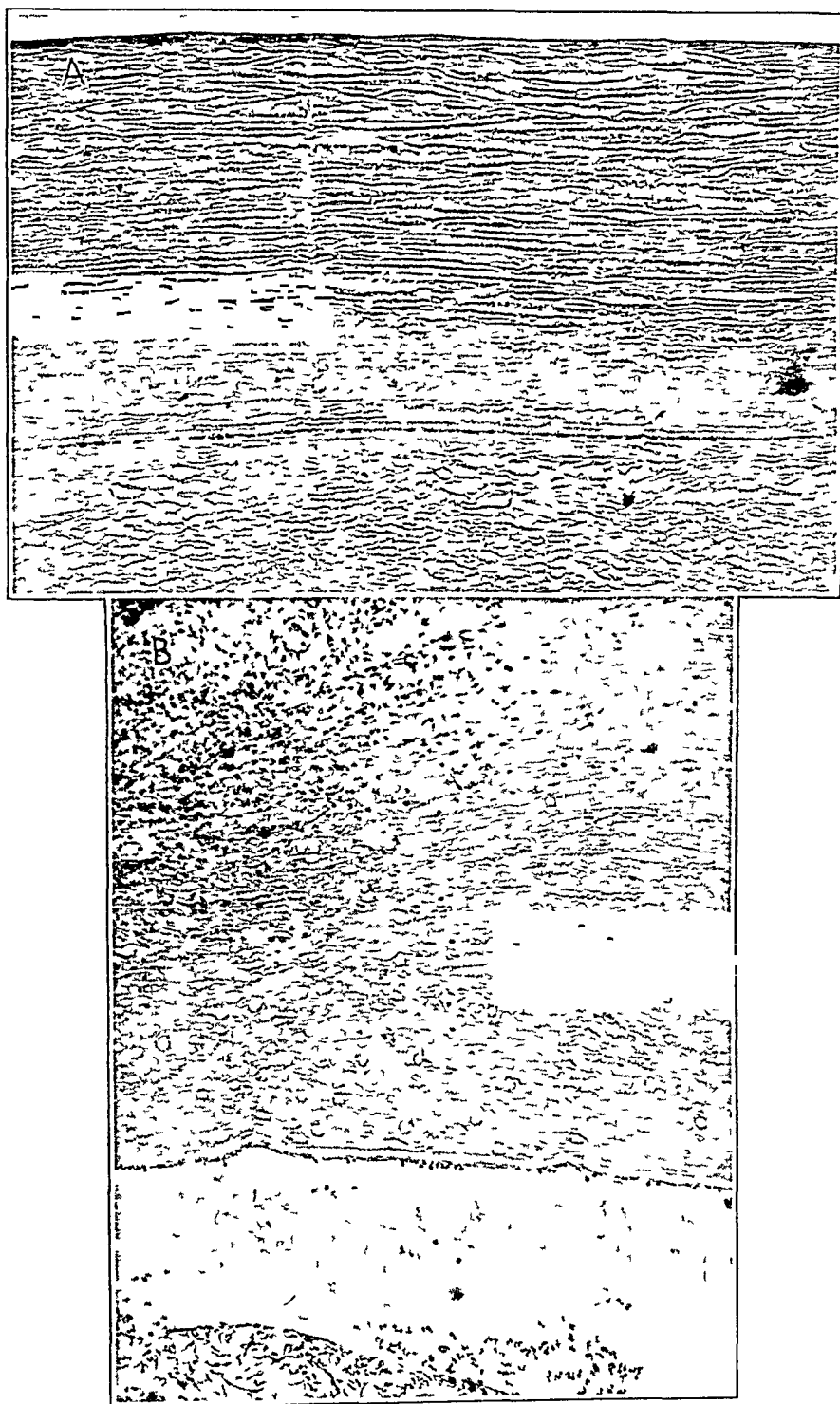


Fig 12—*A*, one hour after exposure. Serous exudation has already appeared in the anterior chamber.  $\times 130$

*B*, within four days after exposure. Polymorphonuclear cells have appeared in the iris, the anterior chamber and the limbal region of the cornea.

(fig 16 A) These new cells had basophilic cytoplasm, with tails and a rather large single nucleus, containing a prominent nucleolus (fig 16 B) Mitoses could not definitely be demonstrated among these cells Sometimes mononuclear wandering cells were present in the tissue at the same time, but a temporal sequence in

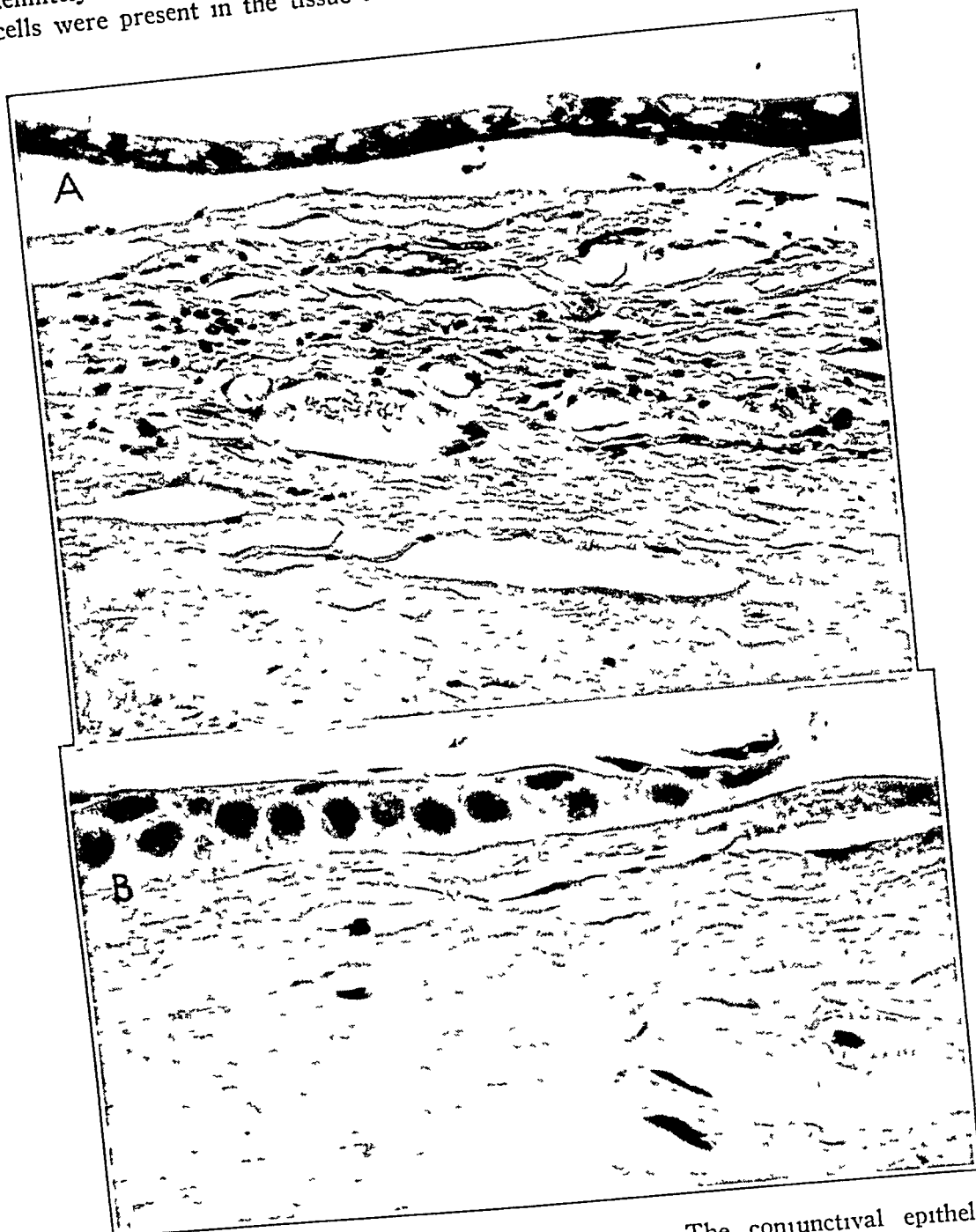


Fig 13—A, twenty-one days after exposure The conjunctival epithelium (containing goblet cells) has grown over the vascularized corneal stroma  $\times 300$

B, section six hours after exposure, showing the tip of corneal epithelium regenerating over the surface of the cornea

the possible transformation of these cells into the new, stroma-like cells just mentioned has not been established These new cells gradually invaded the burned tissue horizontally, but migration vertically was difficult, and at times they lined

up in palisade formation beneath an acellular area, into which they could not penetrate

After several weeks, a severely burned cornea might be seen to be converted into swirls of connective tissue and blood vessels (fig 17 *A*) The central area of burn sometimes showed a tremendous heaping up of scar tissue and vessels, several times the thickness of the normal cornea (fig 17 *B*)

The endothelium, which was rapidly desquamating in areas to which the alkali had penetrated, might be regenerated as early as forty-eight hours later (fig 16 *B*) Reduplication of the layers of new endothelium was common It is

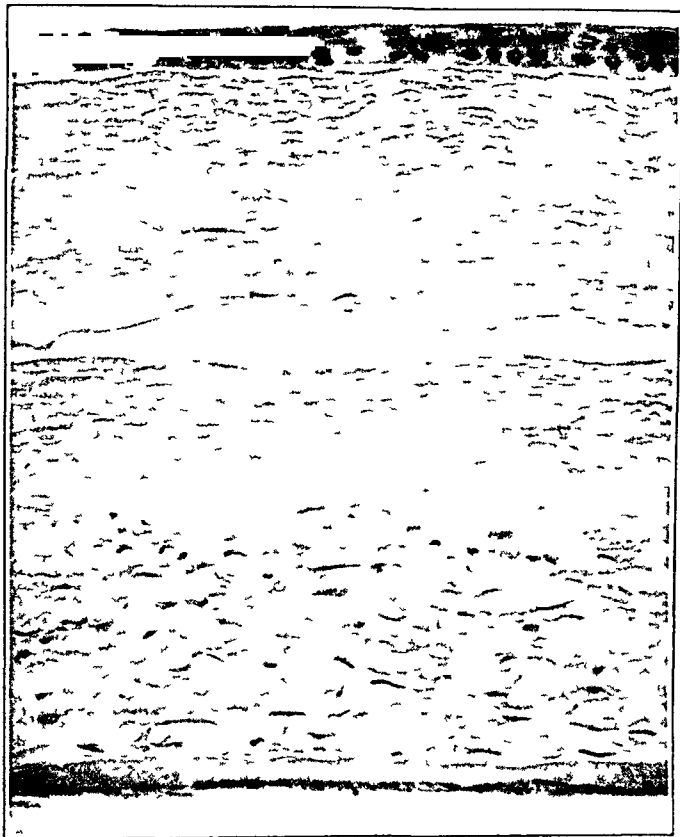


Fig 14—Section of rabbit cornea eight days after the intracorneal injection of 0.1 cc of fiftieth-normal sodium hydroxide The epithelium has regenerated and is partially stratified, remaining adherent to a completely acellular stroma  $\times 300$

to be noted that edema of the corneal stroma might persist for a few weeks after regeneration of the endothelium

#### COMMENT

The proclivity of alkali burns to develop unforeseen complications is well known The statement that alkali burns are progressive in nature generally refers to the observation that the initial cloudiness of the cornea may give no foreboding of the subsequent course and final corneal opacification However, the individual factors which are

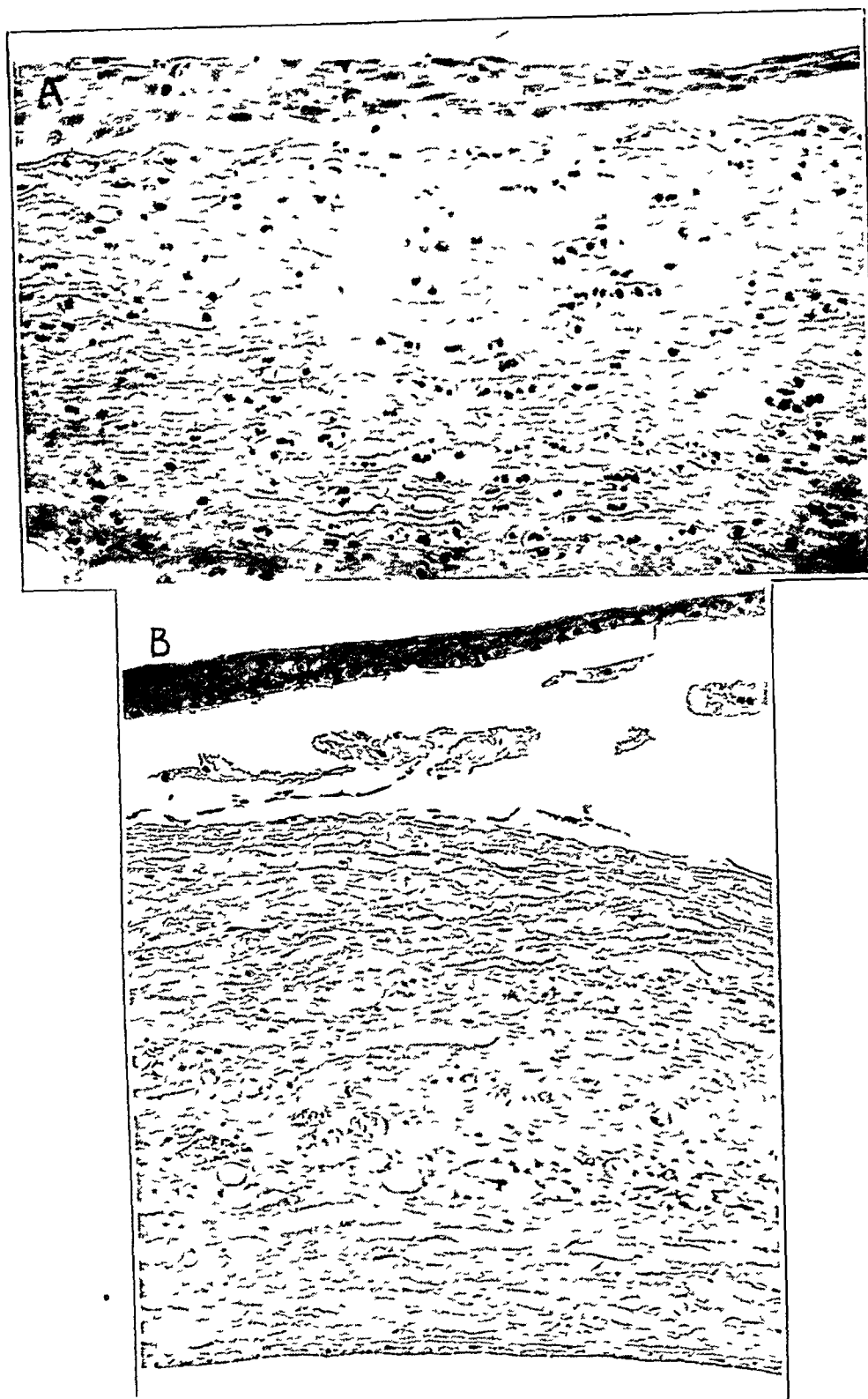


Fig 15—*A*, same eye as that pictured in figure 12 *B*, showing unhealthy regeneration of the corneal epithelium over stroma containing many polymorphonuclear cells

*B*, section of a severely damaged cornea at the end of fourteen days. The corneal epithelium shows irregular and excessive stratification and poor adherence to the underlying stroma. The stroma is heavily vascularized.

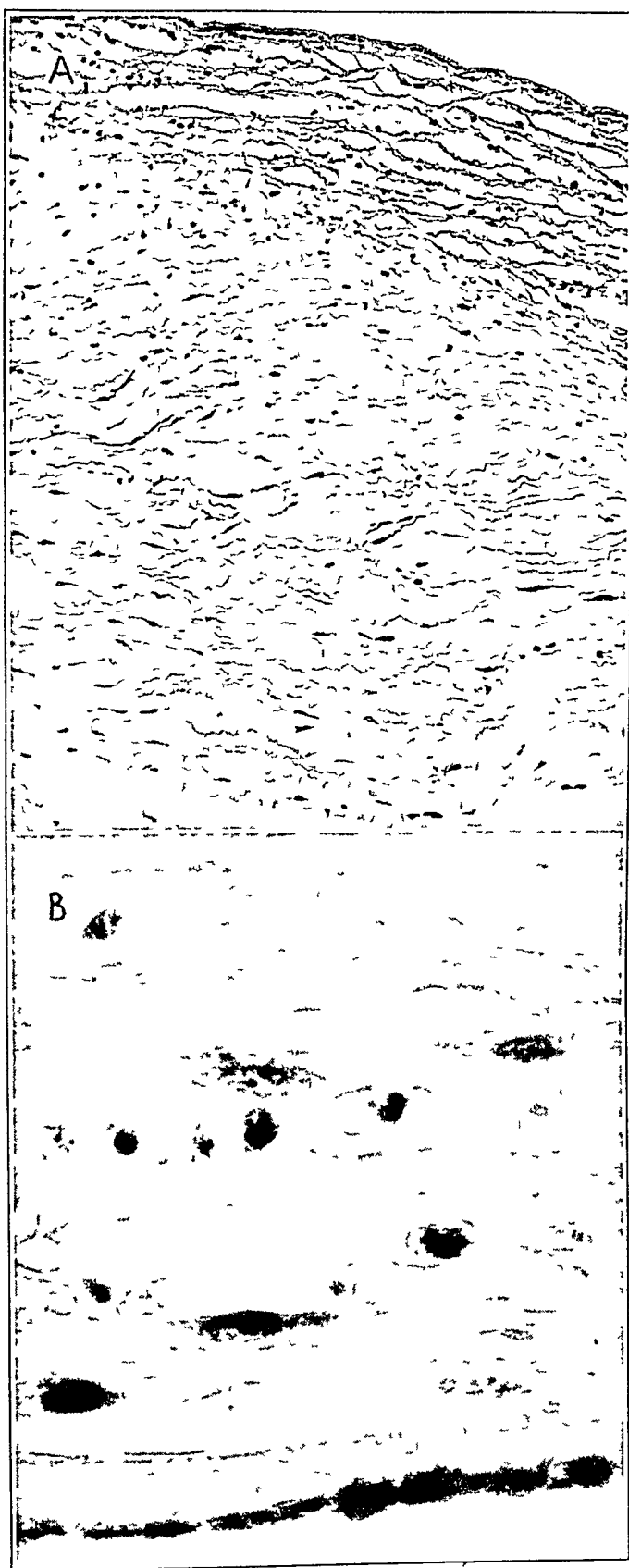


Figure 16  
(See legend on opposite page.)

responsible for the poor visual prognosis may be exceedingly diverse, e. g., corneal infiltrates, secondary infection, ulceration, persistent edema, vascularization, fibrous tissue scarring, growth of a vascularized membrane over the surface of the cornea, staphyloma of the cornea, symblepharon, iritis, secondary glaucoma and cataract. The underlying causes of many of these complications are obscure, but some are certainly interrelated, e. g., (a) destruction of the corneal endothelium, with resulting corneal edema, (b) secondary infection, corneal infiltration and ulceration, although infiltration and ulceration can probably occur without secondary infection, (c) iritis and secondary glaucoma, and (d) desquamation of the conjunctival and corneal epithelium in association with pannus overgrowth of the cornea and symblepharon.

Unlike alkali burns, ocular burns with acids are nonprogressive, and the ultimate prognosis can usually be estimated with accuracy soon after the injury (except for burns with hydrofluoric acid and acids containing heavy metals, such as chromic acid). A comparison of the pathologic changes in acid and alkali burns reveals interesting differences, which suggest more fundamental causes of the complications following alkali burns. These characteristics have been discussed in the literature and have been reviewed previously.<sup>3</sup> The following factors appear to be of etiologic importance.

*Deep Penetrability of the Alkali*—Unlike the condition in acid burns, the corneal epithelium is loosened by alkali within a few minutes and can be wiped off with the slightest amount of trauma. An intact epithelium protects the cornea against injury by substances with a  $p_H$  in the acid range but has little protective effect against substances with a  $p_H$  in the alkaline range.<sup>2</sup> A second factor which reduces the penetrability of acid may be a strong tendency to fixation of the anion by the corneal proteins.<sup>3a</sup> For these reasons, trichloroacetic acid is commonly used for superficial cauterization of the cornea. After the application of this acid the cornea may appear completely opaque, but within a few days the precipitated superficial layers will slough off, leaving entirely clear corneal stroma underneath. Histologically, such delimitation of lesions due to acids has been demonstrated.<sup>3</sup> In contrast to this, alkali

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3 (a) Friedenwald, J. S., Hughes, W. F., Jr., and Herrmann, H. Acid Burns of the Eye, *Arch. Ophth.* **35** 98-108 (Feb.) 1946. (b) Hughes.<sup>1</sup>

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#### EXPLANATION OF PLATE

Fig. 16—*A*, twenty-four hours after exposure. Many new, elongated cells with single, dark nuclei have appeared in the area beneath the severely burned portion.  $\times 130$

*B*, section of the posterior layers of a cornea exposed forty-eight hours previously. The new-formed mononuclear cells have prominent nucleoli and basophilic cytoplasm. The stroma above is completely acellular.  $\times 670$

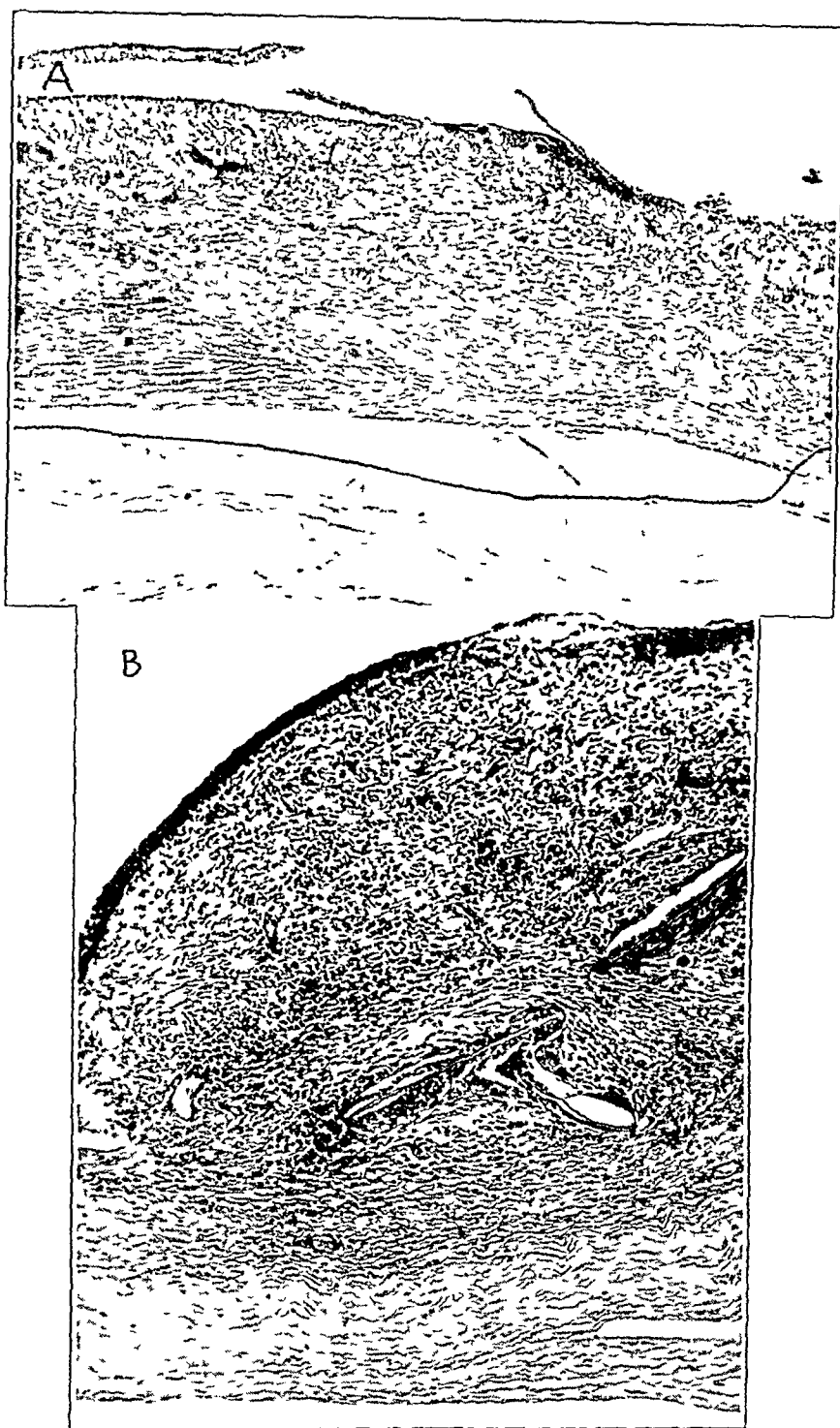


Fig 17—*A*, five weeks after ten minute irrigation with tenth-normal sodium hydroxide. The normal stroma has been replaced with swirls of connective tissue and blood vessels.

*B*, thirty-three days after exposure to twentieth-normal sodium hydroxide. A huge central granuloma has developed, more than doubling the thickness of the cornea in this area.

is said to form soluble albuminates, which do not obstruct further penetration. Ammonia penetrates into the anterior chamber within fifteen seconds after its application to the eye<sup>4</sup> and early histologic evidence of damage to the deeper structures of the anterior ocular segment after exposure to sodium hydroxide has been illustrated.

From the physical considerations of loosening of the corneal epithelium and deep penetrability of alkali, some of the sequelae can be better understood, e. g., secondary infection, which can easily enter the cornea denuded of epithelium, deep corneal necrosis and permanent scarring of the substantia propria, early edema of the cornea secondary to damage of the endothelium, serous exudation into the anterior chamber and ciliary processes, glaucoma secondary to the iritis, perhaps accentuated by the edema of the ciliary processes, and capsular cataract.

*Loss of Corneal Mucoid*—Alkali readily hydrolyzes corneal mucoid. As shown previously, the corneal stroma has a washed-out appearance after irrigation with alkali, and metachromatic staining for mucoid reveals a decrease twenty-four hours after exposure. Acid burns of similar severity show no loss of metachromatic staining at the end of twenty-four hours. Meyer and Chaffee<sup>5</sup> made chemical estimations of hexosamine in corneas exposed to alkalis and acids and found a significant decrease only in the alkali-treated corneas. The possible importance of this difference between acid and alkali burns cannot be evaluated at present.

*Late Corneal Infiltration*—This unpredictable, but not uncommon, complication of alkali burns is one of the causes of relapse in cases in which there is apparent improvement. Polymorphonuclear cells enter the periphery of the cornea within a few hours after injury. This cannot be in response to secondary infection, for cultures of the conjunctival sac are usually sterile for the first twenty-four hours after exposure. It is more likely that a chemotactic substance is produced by the alkaline hydrolysis of the corneal tissue. In preliminary experiments, Friedenwald, Hughes and Herrmann<sup>6</sup> have shown that certain fractions of alkaline hydrolysates of the beef cornea will produce corneal infiltration when injected into the rabbit cornea. The role which secondary infection might play in the development of later corneal infiltration is not clear. In some instances purulent infiltrations and deep corneal ulceration leading to perforation are associated with

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<sup>4</sup> Siegrist, A. Konzentrierte Alkali- und Sauerewirkung auf das Auge, *Ztschr. f. Augenh.* **43** 176-194, 1920.

<sup>5</sup> Meyer, K., and Chaffee, E. Unpublished data, 1942.

<sup>6</sup> Friedenwald, J. S., Hughes, W. F., Jr., and Herrmann, H. Unpublished data, 1942.



purulent conjunctival discharge and endophthalmitis. Such complications are undoubtedly bacterial in origin.

*Necrosis of Limbal Blood Vessels*—Ischemic necrosis of the limbal region readily occurs with alkali burns of moderate severity. The extent to which this contributes to the severity of the associated corneal lesion is uncertain. A few observers<sup>7</sup> have described a corneal lesion secondary to a localized burn of the limbal sclera. It is possible, however, that the application of the acid or alkali might have spread over the surface of the cornea or that the concentration of corrosive used was sufficiently high to penetrate into the cornea or the aqueous from its site of application on the sclera. In the investigation of this question, I injected 0.2 to 0.5 cc. of twentieth-normal sodium hydroxide (the concentration used to produce moderately severe corneal lesions) subconjunctivally and intrasclerally at the limbus in 5 rabbit eyes, in 2 of which injections were made into one-half the limbal circumference. The sclera at the site of the injection became translucent, and the areas of injection became chemotic and ischemic. In none of these eyes, however, did any secondary opacification of the cornea result. Injection of 0.1 cc. of 5 per cent sodium hydroxide in a localized area of the scleral limbus in 3 eyes produced intense corneal opacification and purulent iritis, the corneas perforating after eight days. In view of the penetrating qualities of such a strong solution, it is likely that the alkali diffused into the cornea and the aqueous before it was neutralized by the natural buffering capacity of the tissues.

*Growth of Vascularized Connective Tissue over the Surface of the Cornea*—A fleshy, pterygium-like tongue of tissue frequently grows over the surface of the burned cornea, especially when the adjacent limbal region is involved (fig. 5A and B). In the rabbit this picture does not develop completely, but, as illustrated in figure 12B, the conjunctival epithelium may grow over the surface of the cornea. When a vascularized membrane covers the cornea, later efforts to improve vision by keratectomy or keratoplasty are greatly hampered. When this tissue also forms adhesions with the palpebral conjunctiva, the problem of correcting the symblepharon is added to the difficulties.

*Persistent Corneal Vascularization and Edema*—Occasionally the corneal vascularization following a severe alkali burn becomes intense

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<sup>7</sup> Demig, R. Ueber Ammoniakverletzungen des Auges, *Ztschr. f. Augenh.* **11** 308-311, 1904. Thies, O. Bisher nicht beobachtete Spätfolgen bei Verätzungen des Auges mit Alkalien, *Arch. f. Augenh.* **105** 47-54, 1931. Neumann, J. Frühzeitige operative Behandlung der Augenverätzungen sowie ihre experimentellen und pathologisch-anatomischen Grundlagen, *Klin. Monatsbl. f. Augenh.* **95** 491-515, 1935. Schmelzer, H. Sublimatverätzung des Auges, *ibid.* **90** 184-190, 1933.

and may form nodules of granulation tissue on the surface (fig 18). In addition to the production of irregular astigmatism, the eye frequently remains irritated for months or years. Many times, a low grade edema of the cornea persists. Early in the course of the alkali burn the corneal infiltration and cloudiness seem to clear simultaneously with the ingrowth of blood vessels. However, persistence of corneal vascularization may impair later clearing of the opacity and may possibly be related to late irritability of the eye.

*Recurrent Corneal Ulceration*—One cause of late recurrent ulceration in corneas heavily scarred with corrosive agents has been suggested by Mann and Pullinger,<sup>8</sup> who observed that deposits of cholesterol in

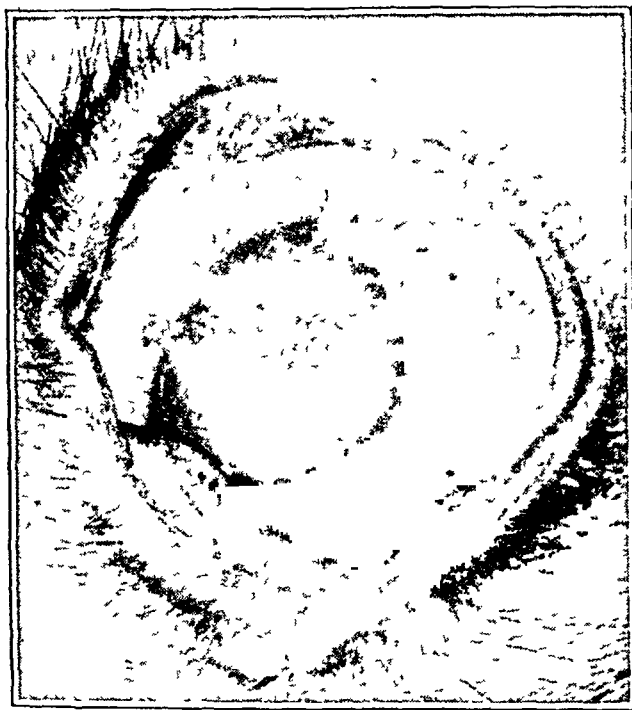


Fig 18—Five weeks after exposure. An elevated mass of vascularized tissue persists in the center of the lesion.

old burns due to mustard gas (dichloroethyl sulfide) erupted through the corneal epithelium. Similar crystalline deposits have been observed in the corneal scars following alkaline burns (fig 3).

*Spontaneous Clearing of the Corneal Opacity*—With the passage of time the corneal scars of alkali burns may show remarkable clearing. The proliferation of spindle-shaped cells in the corneal stroma adjacent to the acellular areas previously exposed to alkali represents an early attempt at regeneration of the stroma cells (fig 16 A and B). There are other conditions in which new cells grow into devitalized, but otherwise uninjured, stroma, resulting in complete transparency of the cornea.

<sup>8</sup> Mann, I. and Pullinger, B. D. A Study of Mustard Gas Lesions of the Eyes of Rabbits and Men, *Proc Roy Soc Med* 35 229-244, 1942, *Am J Ophth* 26:1253-1277, 1943.

This may be seen in the reports on successful grafting of formaldehyde-fixed cornea. Also, burns with solid carbon dioxide result in temporary complete loss of all cellular structures in the affected area, with subsequent regrowth of new stroma cells and ultimate complete restitution of the normal histologic and clinical appearance of the cornea. Therefore, the ulceration, scarring and other late changes which occur after alkali burns cannot be attributed solely to the initial devitalization or loss of all cellular constituents but must be due to some accompanying change in the collagenous or extracellular structure which makes full recovery impossible. Many of the proliferating cells at the edge of alkali-burned areas probably finally become fibroblasts.

#### SUMMARY

Studies were made of the clinical and pathologic course of sodium hydroxide burns of the rabbit eye and of the clinical observations on alkali burns in human eyes. The course of an alkali burn may logically be divided into three stages, with the following prominent characteristics:

*Acute Stage*—This stage consists in ischemic necrosis and edema of the conjunctiva and limbal region of the sclera, sloughing of the corneal epithelium, histologic evidence of rapid and deep penetration of the alkali with necrosis of cells in the corneal stroma and endothelium, loss of corneal mucoid, edema of the corneal stroma and ciliary processes, infiltration of polymorphonuclear cells into the cornea and iritis.

*Reparative Stage*—This stage includes the subsidence of conjunctival and corneal edema, regeneration of the conjunctival and corneal epithelium, vascularization of the cornea, clearing of the corneal opacification, proliferation of elongated mononuclear cells at the periphery of the burned area in the corneal stroma, regeneration of the corneal endothelium and disappearance of the iritis.

*Stage of Late Complications*—At this stage there may be localized corneal infiltrations, progressive or recurrent corneal ulceration, overgrowth of the cornea with a vascularized membrane, permanent corneal opacification, staphyloma of the cornea, persistent or exudative iritis, secondary glaucoma, cataract or symblepharon.

Unlike the nonprogressive course of acid burns, alkali penetrates rapidly and deeply into the anterior ocular segment, and mucoid disappears from the involved corneal stroma.

The possible causes and significances of leukocytic infiltrations into the cornea, necrosis of the limbal blood vessels, overgrowth of the cornea with vascularized connective tissue, persistent corneal vascularization, recurrent ulceration and spontaneous clearing of the cornea are discussed briefly.

# ANIMAL OPERATING EQUIPMENT FOR EXPERIMENTAL OCULAR SURGERY

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NEW YORK

MY ASSOCIATES and I were confronted with the problem of devising an operating setup for experimental surgery which would be suitable for operating on the eyes of small animals, particularly rabbits. The apparatus which I am about to describe was homemade, is rather simple in construction and has been very satisfactory. We felt that it would be worth while to offer this description.

The table is made out of a rectangular slab of hardwood mounted on an elevating table. We used the elevating table of a Zeiss slit lamp, so that the swinging arm could also be utilized. All the parts that fasten to the hardwood table are easily removable, for cleaning. The animal is immobilized by means of four clamps which hold the paws, two side boards that lie alongside the flanks and a U-shaped neck piece. A hammer lamp mounted on a gooseneck is fastened to the side of the table in such position that the spotlight falls on the operative field. To the swinging arm of the elevating table is attached a metal crossbar, which supports a binocular dissecting microscope or a camera.

## DETAILS OF CONSTRUCTION

The hardwood slab is 31 by 13 by  $\frac{3}{4}$  inch (78 by 33 by 1.9 cm) and is provided with slots and holes that accommodate the removable parts. The clamps used to immobilize the paws are made crotch shaped, are lined with sponge rubber and lock shut by means of a metal hinge adapted for the purpose. These clamps are  $1\frac{3}{4}$  by  $1\frac{3}{4}$  inches (4.5 by 4.5 cm) and 1 inch (2.5 cm) thick, with inside measurements of  $\frac{7}{8}$  by  $1\frac{1}{4}$  inches (2 by 3 cm), and the round base peg is  $\frac{7}{8}$  inch in diameter. The neck piece is  $3\frac{1}{4}$  by  $3\frac{1}{4}$  by 1 inch (8 by 8 by 2.5 cm) in outside dimensions and  $2\frac{1}{8}$  by 3 inches (5.4 by 7.6 cm) in inside dimensions. The base of the neck piece locks into a slot in the hardwood table and is fastened with a hook and eye catch. A cord passes through slots on the free ends, to hold the neck of the rabbit. The side boards are 2 by  $5\frac{1}{4}$  inches (5 by 13 cm) and  $\frac{3}{8}$  inch (0.95 cm) thick. They are fastened to the table with two 3 inch (7 cm) nails, which slide into holes in the table and are locked in position with hook and eye catches. A cord is provided that passes over the side boards, to hold the body of the rabbit.

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This study was made under a grant from the Ayer Foundation.

From the Corneal Research Laboratory of the Manhattan Eye, Ear and Throat Hospital.

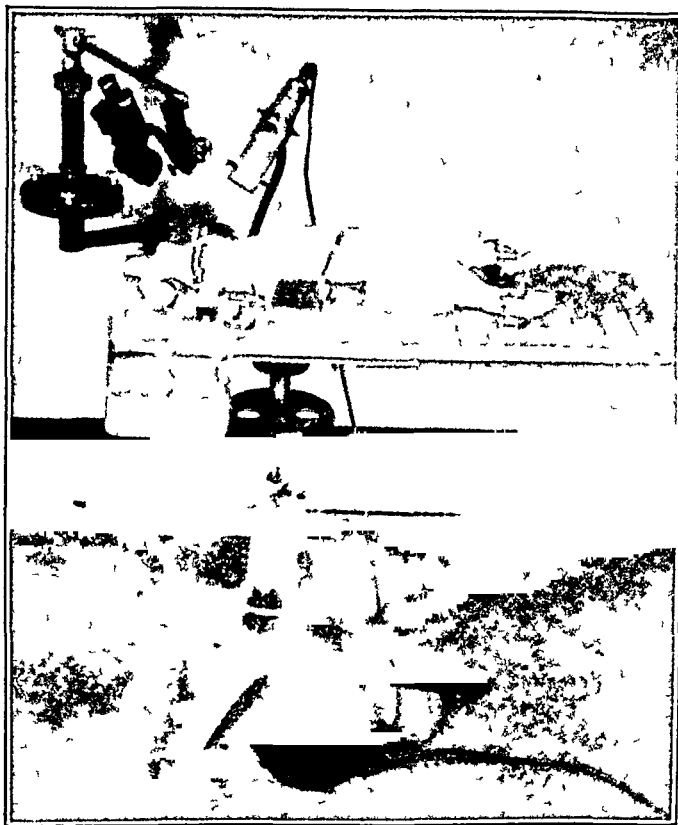


Fig 1—Over-all picture, showing table, lamp and binocular microscope on the swinging arm

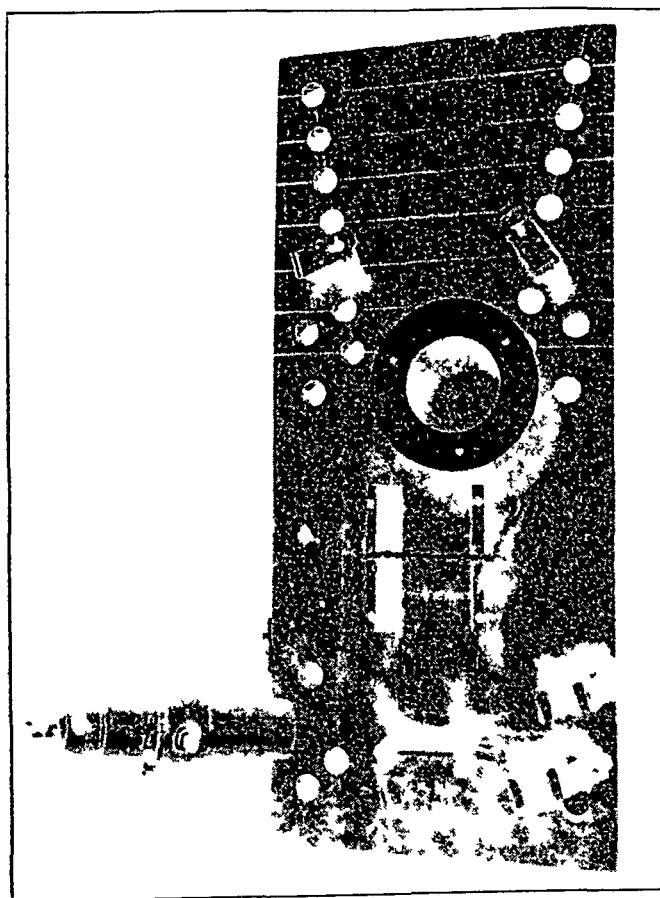


Fig 2—Table top viewed from above, showing the circular hand rest.

The position of the neck piece is stationary, as is that of the side boards, but the paw clamps may be shifted about into the holes provided, depending on the size of the animal.

The head of the rabbit is immobilized with two U-shaped  $\frac{1}{8}$  inch (0.32 cm) wires. The free ends of each wire are passed through holes in the wooden table, so the top holds the rabbit's head. One is curved to fit along the back of the head, the other passes through the mouth like a bit and over the nose.

An aluminum pan 7 by  $12\frac{1}{2}$  by  $2\frac{1}{2}$  inches (17.5 by 31.5 by 6 cm) is suspended by a short chain beneath the upper end of the table, for waste material.

To furnish a hand rest while the surgeon is operating, a three-legged, round aluminum table with a hole in the center is provided, which fits under the drape.

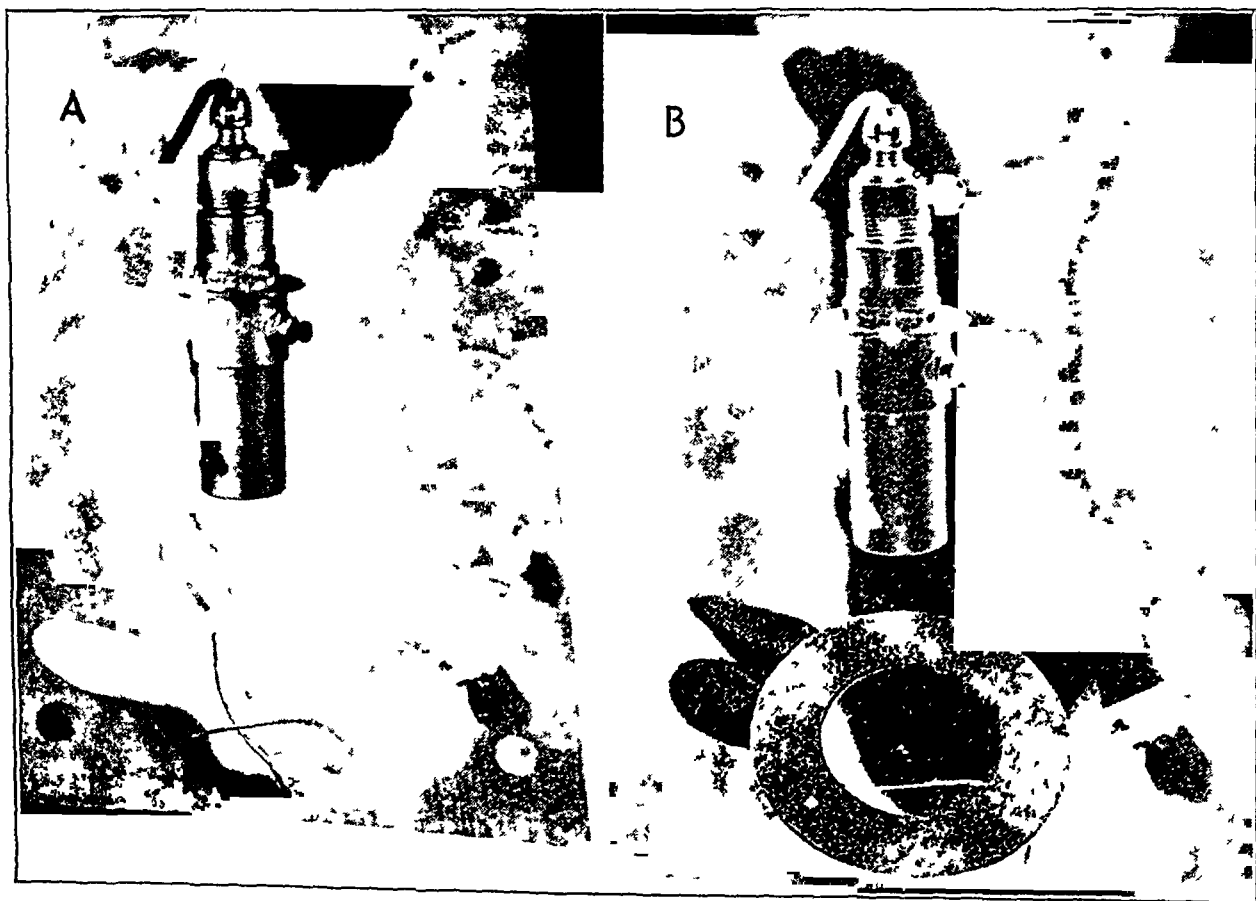


Fig 3—A, animal in operating position, showing the wires that immobilize the head. B, hand rest in position. The drape is placed over this.

This table is 6 inches (15.3 cm) in outside diameter,  $3\frac{1}{2}$  inches (9.9 cm) in inside diameter and  $\frac{1}{8}$  inch (0.32 cm) thick and is mounted on  $2\frac{1}{4}$  inch (5.5 cm) legs.

Fixation of the rabbit's eyeball is achieved by passing four equidistant 0000 braided silk atraumatic sutures through the limbus and winding them around cleats of an aluminum disk. This disk is  $4\frac{1}{4}$  inches (10.8 cm) in outside diameter,  $2\frac{1}{4}$  inches (5.7 cm) in inside diameter and  $\frac{1}{64}$  inch (3.9 mm) thick. These sutures effectively hold the eyelids out of the field, so that no lid retractor is necessary.

## METHOD OF OPERATION

The rabbit is completely immobilized on the table until it has been put to sleep with sodium pentobarbital injected intravenously, in a dose of approximately 10 mg per pound of body weight. Then the neck clamp is removed, and the two U-shaped wires are put into their respective positions, to hold the head. The operative area is then painted with a 1:1,000 solution of zephiran chloride, and 2 per cent solution of procaine hydrochloride is injected into the conjunctival surface of the lids and behind the eyeball. The hand rest is then put in place and the sterile sheet draped over the field. The fixation sutures are placed



Fig 4—Fixation of the eyeball by means of sutures passed through the limbus and fastened to cleats on the metal disk. This disk is supported by the hand rest under the drape.

radially, superficially in the limbus, and wound around the cleats of the aluminum disk.

The operator controls the position and focusing of the dissecting microscope by means of a sterile rubber cap, which covers the focusing knob.

## COMMENT

The use of local injection of procaine, as well as intravenous injection of pentobarbital, has greatly improved our anesthesia. There

is great individual variation in the effect of intravenously administered anesthetics in rabbits, when we depended on them alone, too often the anesthesia was either too deep or too light. Our technic now is to use the barbiturate as a basal anesthetic and to rely on procaine for complete blocking of pain sensation. These drugs are mutually antagonistic so far as any toxic effect is concerned. The lids are anesthetized, in order that they may be sewn together for protection when the operation is completed.

Our method of fixation of the eyeball was worked out for the cornea-grafting operation. These sutures are removed at the completion of the operation, and they do no harm. If intraocular operation is to be performed, three, instead of four, such sutures can be used and they should be placed slightly farther back, beyond the limbus. For other types of operation, the sutures may be passed through the lids and the nictitating membrane instead. We use the sutures over and over, resterilizing them by soaking in antiseptic solution (zephiran chloride, 1:1,000).

#### SUMMARY

Animal operating equipment and the methods used for experimental ocular surgery on the rabbit are presented. The equipment described has been used in hundreds of operations and has been entirely satisfactory in our hands.

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# SCOTOMA AS A COMPLICATION OF DECOMPRESSION SICKNESS

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BERKELEY, CALIF

EARLY attention to physiologic disturbances on ascent to high altitudes was directed to the effects of decreased partial pressure of atmospheric oxygen. The elimination of this factor with the use of modern oxygen equipment has disclosed new aspects of the situation no less serious in the development of full utilization and effectiveness of present and future aircraft in war and commerce.<sup>1</sup>

When men are exposed to low barometric pressures equivalent to altitudes greater than 25,000 feet (7,500 meters), symptoms of decompression sickness frequently appear. These symptoms become commoner and severer with increases in altitude and physical activity<sup>2</sup> and are not due to inadequate oxygen content of the inspired air.<sup>3</sup> The commonest symptoms are joint pains (aviator's "bends"), thoracic symptoms ("chokes"), headache, abdominal gas pain, hyperventilation, muscular pain, dizziness and syncope, neurocirculatory postflight reactions also occur.<sup>4</sup> Any of these symptoms may prove disabling.

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From the Aero Medical Unit of the Division of Medical Physics and Medicine, University of California.

The work described in this paper was done under the direction of Dr J H Lawrence, under a contract recommended by the Committee on Medical Research, between the Office of Scientific Research and Development and the University of California.

1 Lawrence, J H. Aviation Medical Problems with Special Reference to Altitude Pain, *J Nerv & Ment Dis* **99** 703-711 (May) 1944.

2 Cook, S F, Williams, O L, Lyons, W R, and Lawrence, J H. A Comparison of Altitude and Exercise with Respect to Decompression Sickness, *War Med* **6** 182-187 (Sept) 1944.

3 Engle, G L, Webb, J P, Ferris, E E, Jr, Romano, J, Ryder, H, and Blankenhorn, M A. A Migraine-Like Syndrome Complicating Decompression Sickness, *War Med* **5** 304-314 (May) 1944.

4 (a) Bridge, E V, Henry, F M, Cook, S F, Williams, O L, Lyons, W R, and Lawrence, J H. Decompression Sickness, *J Aviation Med* **15** 316-327 (Oct) 1944. (b) Bridge, E V, Henry, F M, Williams, O L, and Lawrence, J H. "Chokes" A Respiratory Manifestation of Aeroembolism in High Altitude Flying, *Ann Int Med* **22** 398-407 (March) 1945. (c) Goggio, A F, and Houck, G H. Physiologic Abnormalities and Pathologic Changes Following Exposure to Simulated High Altitudes, *War Med* **7** 152-156 (March) 1945.

In addition, defects in the field of vision during and after exposure are sometimes observed. Negative scotoma (an area of complete absence of vision without irritative phenomena, such as color and lights) ordinarily appears first. Later there is a positive scotoma, involving white or colored dancing spots; shimmering, wavy lines, and the like (scintillating scotoma). After increasing in intensity, the scotoma invariably recedes peripherally, and contralateral headache usually follows. The visual symptoms occur at altitude or after descent, invariably they occur with or after "bends" or "chokes."<sup>3</sup> Recent British work on the subject has been reported by Livingston.<sup>5</sup> Casual observations have been made in this laboratory, and 3 cases have been recorded in an unpublished report by Atkinson.<sup>6</sup> In order to add to the number of observed cases and to suggest the importance of certain observations not previously emphasized, this report is presented.

#### METHOD

In this study, 41 medical students from 20 to 29 years of age were exposed to lowered barometric pressure in a decompression chamber a total of 100 times. Ascents were to simulated altitudes of 35,000 and 38,000 feet (10,600 to 11,500 meters) at a rate of 3,000 feet (900 meters) per minute. Since comparison of the results obtained at the two altitudes disclosed no significant differences, no separation of the groups will be made. Pure oxygen was supplied from a pressure line through constant flow masks at altitudes above 10,000 feet (3000 meters). Exposure to high altitude lasted ninety minutes unless symptoms were so severe that earlier descent was necessary for reasons of safety, such subjects were returned to normal pressure in an airlock. Since other aspects of high altitude physiology were being simultaneously investigated, various arm and leg exercises were performed by the subjects while at altitude.

Central visual fields were charted on a 1 meter, 35 degree field Bjerrum screen with a 3 mm white test object before ascent and at ten minute intervals after descent. Ophthalmoscopic observations on the fundi were made immediately after descent, with special emphasis on comparison of the retinal vessels with their preascent state.

#### OBSERVATIONS

Of the 100 observed ascents, 37 involved descent to sea level because of "bends" or "chokes" and related symptoms. In 4 ascents the subjects were removed from the chamber for such disqualifying reasons as gas pains, while in the remaining 49 ascents no symptoms occurred severe enough to make descent advisable before the regular termination of the run.

Visual disturbance, scotoma or headache occurred only as a result of ascents terminated by severe decompression sickness. Of these 37

<sup>5</sup> Livingston, P. C. Visual Problems of Aerial Warfare, *Lancet* 2.67-73 (July 15) 1944.

<sup>6</sup> Atkinson, M. The Effects of High Altitude on the Visual Apparatus, Anatomy Records (unpublished), University of California, November 1944.

ascents, 18 resulted in symptoms of visual disturbance or headache (table 1). Of these 18 ascents, 4 involved blurred vision for several hours, and 14 ascents, headache of twenty minutes to forty-eight hours' duration, after descent (table 1). On 7 of these runs (5 men on 7 of 11 ascents) scotomas were manifested after descent, and on 1 other ascent (1 man, 1 of 4 ascents) symptoms which were presumably scotoma disappeared suddenly on descent to 9,000 feet (2,700 meters). All these subjects reported headache after descent.

TABLE 1—*Visual Symptoms and After-Effects*

| Visual Symptoms                   | No. of Ascents |
|-----------------------------------|----------------|
| Lacrimation                       | 2              |
| Blur at altitude                  | 3              |
| Difficulty in focusing (not blur) | 2              |
| "Heat waves"                      | 2              |
| Headache at altitude              | 6              |
| Dizziness                         | 3              |
| Visual After Effects              |                |
| Blurring                          | 4              |
| Headache                          |                |
| Diffuse                           | 2              |
| Bilateral frontal                 | 12             |

The scotomas were characteristically bilateral and homonymous but not congruous, they disappeared by drifting at various speeds across the field in a generally counterclockwise, centrifugal manner, to leave the periphery of the 35 degree tangent screen in ten to forty-five minutes, rather smaller in diameter. Two men reported disturbances in the right field at altitude, and similar defects were charted in the left field after descent. One man manifested a monocular scotoma, which shrank and disappeared without moving.

TABLE 2—*Incidence of Symptoms*

|   |                        | Percentage |
|---|------------------------|------------|
| In 100 exposures                          | Decompression sickness | 40         |
|   | Visual symptoms        | 20         |
|   | Scotomas               | 7          |
| In 40 instances of decompression sickness | Visual symptoms        | 50         |
|   | Scotomas               | 20         |
|   |                        |            |
| In 20 instances of visual symptoms        | Scotomas               | 40         |

The field defects, when first charted, varied in size from about 5 by 10 degrees to 15 degrees in width and extended through a full half of the binocular field, exclusive of the macular area. While the defects were usually of the same general size and position in the fields of the two eyes, they were not identical. In 1 case two separate defects were manifested in the left upper quadrant of the left field, while the right field showed one defect in each of the upper left, upper right and lower

ight quadrants In 2 other cases small scotomas, isolated from the chief defect, were manifested in the field of one eye which could not be demonstrated in the field of the other eye In no case did a scotoma approach closer than 5 degrees to the fixation point

No significant changes in the physiologic blindspot were manifested with the target used

Ophthalmoscopic examination disclosed nothing significant in the media, fundi or pupillary reflexes

#### COMMENT

The following significant characteristics of these scotomas were noted (1) bilateral homonymous, incongruous type, (2) consistent sparing of the macular area, (3) disappearance by centrifugal drifting, with diminishing size, and (4) frequent involvement of both horizontal and vertical hemifields

Localization of a single lesion which could be justified in view of the several factors which must be considered is difficult The drifting nature of the field defect suggests local anoxia due to a vascular defect That this is aeroembolism or local vasoconstriction due to direct irritation by nitrogen bubbles is not acceptable because the scotomas often develop during or after descent, and when onset was at altitude the subjective severity, with a single exception, increased, rather than decreased, with descent This is, of course, in contradistinction to the symptoms of "bends," which are relieved to a notable degree by small increases in atmospheric pressure That toxic products liberated elsewhere and carried in the blood stream (an occurrence which has been suggested as a factor in the production of decompression sickness) could cause local angiospasm is a possibility already suggested<sup>3</sup>

Location of the lesion in the retinal vessels is not easily compatible with the generally homonymous character of the scotomas or with the lack of observable ophthalmoscopic signs The known high susceptibility of cortical tissue to anoxia, the larger macular and paramacular areas of representation in the cortex and the peripheral, rather than central, drifting of the field defect suggest a location in the calcarine cortex Inconsistent with this, however, is the continuity of the defect across the vertical midline Progression of the scotomas through as much as 270 degrees of the field has been noted, and that this is of frequent occurrence not only is indicated by our observations but is confirmed by reference to illustrations accompanying previous reports Only a chiasmic lesion, not compatible with other observed signs, seems to explain this phenomenon The danger to life of interference with cerebral vascular supply is self evident, yet, as has been pointed out,<sup>4c</sup> deaths in many thousands of ascents have been extremely rare

It is felt that correlation of the visual phenomena with other observed reactions of the central nervous system and study of the basic mechanism of decompression sickness as a whole are necessary to a satisfactory consideration of the visual phenomena

The correlation between appearance of scotomas and migraine observed by Engel and his co-workers<sup>3</sup> and by Livingston<sup>5</sup> was not noted in this series, since but 1 of the 5 men had a history, personal or familial, of migraine or possible migraine

#### SUMMARY

Central visual fields were charted for 41 men on 100 ascents. Of this number, 28 men on 37 ascents suffered from decompression sickness.

Ten men on 18 of 34 ascents manifested various visual symptoms or headache.

Five men on 7 of 11 ascents manifested scotomas. One man on 1 of 4 ascents had a probable scotoma, which disappeared during descent.

There was no correlation of the occurrence of scotoma and a history of migraine.

Significant characteristics of the scotomas were (1) bilateral homonymous, incongruous type, (2) macular sparing, (3) peripheral drifting and (4) continuity across the vertical midline.

Identification of the causative lesion is not at present possible.

University of California, Donner Laboratory (4)

## Clinical Notes

### INSTRUMENT FOR LOCATING RETINAL RUPTURES DURING OPERATION

A HAGEDOORN, M D, AMSTERDAM, NETHERLANDS

IT is necessary to check the supposed projection of a retinal rupture, or tear, on the surface of the sclera during the operation. This is done either with pupillary or with scleral transillumination. In using the latter method, I found Goldmann's<sup>1</sup> instrument very satisfactory.

It consists of a small metal cover with tiny, sharp teeth, which, with a rotating movement, fix the cover to the sclera. Subsequently, a very small electric lamp is inserted in it. The light of this little lamp is completely masked by the metal cover, except for the beam passing through a small hole in the flat surface of the metal cover, adjacent to the sclera wall, which can be detected ophthalmoscopically.

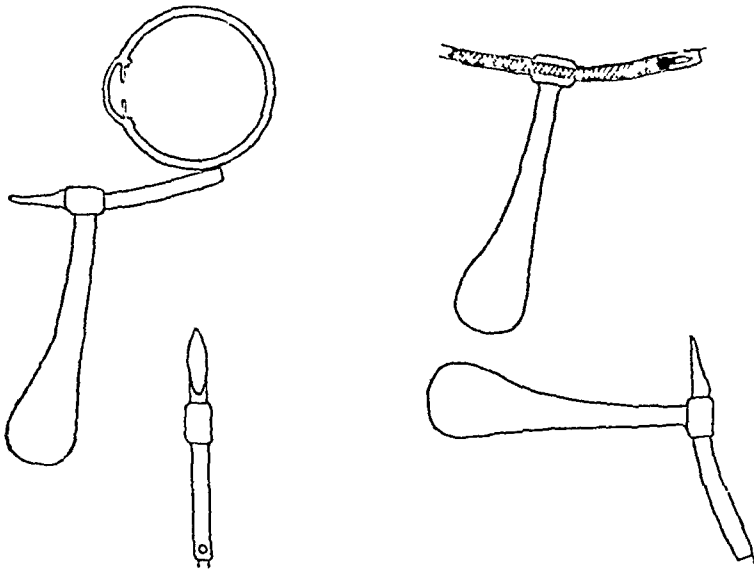


Fig 1—Drawings showing the instrument for locating retinal ruptures during operation

The relative position of the spot of light of the transilluminator and the rupture indicate the error in localization, which with this method can easily be estimated and corrected.

Though this method proved to be excellent in many cases, it requires a skilled and careful assistant because of the following disadvantages: First, the eye must be brought into position for ophthalmoscopic examination with another instrument, the forceps; second, the metal cover may become detached from the sclera; third, the fixation of the little instrument is not always easy, and a few adjustments may take much time.

<sup>1</sup> Goldmann, H. Ein einfaches Instrumentchen zur exakten Netzhautlochlokalisation, *Klin Monatsbl f Augenh* 97 254, 1936

Various instruments have been made by the instrument maker Buighardt to do away with these disadvantages. Finally, the instrument, as shown in figure 1, was devised and proved satisfactory.

Like Goldmann's instrument, the size of the hole is about 0.8 mm. The fine needles are easily and safely anchored in the sclera. A forceps is not necessary, and the instrument is even more safely fixed to the scleral wall as the bulb is rotated into position for ophthalmoscopic inspection. The assistant has only to take care that the wing of the instrument is directed toward the center of the cornea and that the flat side of the wing is parallel with the axis of the eye. Thus the instrument itself is an additional aid in estimating the situation of the meridian of the hole. To detect the projection of a hole at the posterior pole, a somewhat longer instrument was made (fig. 2), and my colleague and I have a number of such in the operating room, of various curvatures, lengths and sizes of openings, through which the eye is transilluminated. Generally we use the instrument shown in figure 1. We also had a model which was open at the end, so

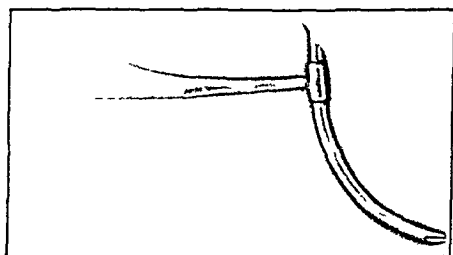


Fig. 2—Instrument for detection of a hole at the posterior pole

that it illuminated a larger part of the fundus, but in 1 case this gave rise to confusion, since a detached retina makes observation less accurate.

In a case of neglected perforating injury, in which a small piece of iron had been firmly fixed in the sclera for many months and could not be removed with the giant magnet, the open model was used. The beam of light from the open end of the transilluminator was brilliantly seen, since there was no complicating detachment of the retina, and the small round light spot was separated from it by a small, dark streak. With a change in the position of the localizer, a spot could be found in which the small round light was invisible, the hole in the metal cover lying exactly on the small piece of iron. During the operation the iron was found precisely at that point, so that the operation took little time and was very simple.

### CLOSTRIDIUM WELCHII PANOPHTHALMITIS

#### Report of a Case

CAPTAIN BERTRAM CAPUS, MEDICAL CORPS, ARMY OF THE UNITED STATES

**C**LOSTRIDIUM (*Bacillus*) *welchii* panophthalmitis is a rare infection of the eye. The last report in the literature, by Walker,<sup>1</sup> mentioned 12 previous cases and presented an adequate review of the

<sup>1</sup> Walker, S., Jr. Prognosis of *Bacillus Welchii* Panophthalmitis, *Arch Ophth* 19 406 (March) 1938.

literature The following new case of *Cl welchii* panophthalmitis is presented for addition to the literature

#### REPORT OF CASE

A soldier aged 28 was injured on Feb 24, 1945 by the explosion of a wooden mine Examination at the evacuation hospital revealed multiple superficial lacerations of the face and a penetrating injury of the left eye His facial wounds were debrided and sutured, and a dressing was applied to his left eye He was prepared for evacuation to a general hospital for further treatment

*February 26*—The patient arrived at the general hospital, less than forty-eight hours after the injury During this period he had received 160,000 units of penicillin intramuscularly and 1 Gm of sulfadiazine every four hours Examination on admission revealed that the patient was in severe pain and was dehydrated and toxic, with a temperature of 102 F and a pulse rate of 100 per minute

*Left Eye* There was no light perception or projection, the globe was immobile, proptosed and extremely tender, and there were pronounced chemosis and edema of the lids, making adequate examination impossible

*Right Eye* Vision was 20/40 Numerous subconjunctival foreign bodies and corneal abrasions were noted Examination of the interior of the eye revealed no foreign bodies or hemorrhages

The patient was prepared for operation the following morning by intravenous administration of fluids, sedation for pain and administration of 20,000 units of penicillin every three hours and 1 Gm of sulfadiazine every four hours

*February 27*—On examination, with the patient under sodium pentothal anesthesia, the left eye showed marked chemosis and proptosis, and the cornea was cloudy, with a horizontal laceration, 3 mm long, extending nasally to the limbus, its edges gaped slightly, but there was no prolapse of the ocular contents Slight pressure on the cornea resulted in a gush of coffee-colored exudate and gas with a characteristic odor Evisceration was performed, and within the liquefied necrotic contents was found an irregular piece of wood, measuring 3 by 3 by 5 mm No lens or uvea could be recognized as such Material was taken for culture and identification of the organism, and the wound was left open The right eye showed no change from the previous examination The sutured facial wounds were infected and were opened, and the same coffee-colored exudate was found in them Material was taken for culture

*Postoperative Course*—The patient was given 180,000 units of tetanus-gas gangrene antitoxin intravenously Within twenty-four hours the temperature returned to normal and he was free from systemic signs of toxicity Within ten days all exudation from the scleral cavity ceased, and the facial wounds healed by secondary intention A delayed closure of the conjunctiva was performed, and healing occurred without complications

*Laboratory Studies*—Smears and cultures revealed a gram-positive bacillus, with all the cultural and morphologic characteristics of *Cl welchii*

#### COMMENT

In this case it is of interest to note that *Cl welchii* infection occurred despite the early systemic use of penicillin and sulfadiazine Light is thrown on this type of infection and its failure to respond to the therapy



employed by the following experimental work Von Sallmann<sup>2</sup> and Chiazzaro,<sup>3</sup> working with rabbits, showed that *Cl welchii* panophthalmitis can be produced only by injection of the organisms into the lens or the vitreous. Injection into the anterior chamber produces only transitory iritis. The work of Bellows and Chinn<sup>4</sup> and von Sallmann and associates<sup>5</sup> has shown that both the sulfonamide compounds and penicillin fail to enter the vitreous in any appreciable quantity.

#### CONCLUSION

Another case of *Cl welchii* panophthalmitis is presented for record.

*Cl welchii* panophthalmitis is probably rare, for the organism must be introduced into the lens or the vitreous to set up panophthalmitis.

The prophylactic use of systemically administered penicillin and the sulfonamide compounds is of questionable value because of the failure of these drugs to enter the vitreous in appreciable quantities.

1749 Grand Concourse, New York

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2 von Sallmann, L. Penicillin and Sulfadiazine in the Treatment of Experimental Intraocular Infections with *Staphylococcus Aureus* and *Clostridium Welchii*, *Arch Ophth* **31** 54 (Jan) 1944

3 Chiazzaro, D. Les infections oculaires par microbes anaerobies, *Ann d'ocul* **169** 953 (Dec) 1932

4 Bellows, J., and Chinn, H. Penetration of Sulfathiazole in the Eye, *Arch Ophth* **25** 294 (Feb) 1941

5 von Sallmann, L., Meyer, K., and Di Grandi, J. Experimental Study of Penicillin Treatment of Ectogenous Infection of the Vitreous, *Arch Ophth* **32** 179 (Sept) 1944

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## News and Notes

EDITED BY DR W. L. BENEDICT

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#### GENERAL NEWS

**The Treacher Collins Prize Essay**—Under this title, the Council of the Ophthalmological Society of the United Kingdom has instituted a prize of £100, awarded triennially, for the best essay submitted on a subject selected by the council.

The prize shall be open to qualified medical practitioners of any nationality.

The essay shall be written in the English language.

The subject for the next award of the prize is "Nutritional Eye Disease."

The closing date for sending in essays for this award is Dec 31, 1947. Essays should be submitted to the honorary secretary, Ophthalmological Society of the United Kingdom, 5 Racquet Court, Fleet Street, E.C. 4, London, from whom also any further particulars can be obtained. No name should be on any essay, but a distinguishing pseudonym or quotation should be used. This should also appear on a sealed envelope containing the candidate's name and address. This envelope should accompany the essay.

## Correspondence

### THIAMINE (VITAMIN B<sub>1</sub>) IN OPHTHALMOLOGY

To the Editor —Not until in March 1946 did I, living in now liberated Netherlands, enjoy the opportunity of reading the American medical periodicals, therefore, the interesting note, entitled "Thiamine (Vitamin B<sub>1</sub>) in Ophthalmology," by Dr. V. Everett Kinsey, published in the ARCHIVES (26: 129-130 [July] 1941), has not come to my attention until now

Unfortunately, there seems to be some misunderstanding about my findings, on the one hand, and the results obtained by other investigators, on the other. To clarify these apparent contradictions, and to enable the American reader to compare my statements with what Kinsey believes to be my statements, I wish to translate a few sentences from my papers published in 1938. In *Archives d'ophtalmologie* (2: 108 [Feb.] 1938) I wrote.

*Nous basant sur un grand matériel de cristallins fort différents, nous avons pu aisément trouver la quantité en vitamine B<sup>1</sup> contenu dans un seul cristallin.*

*Dans ces conditions, il est naturellement impossible de doser la vitamine B<sup>1</sup> dans un seul cristallin, qu'il soit normal ou pathologique.* (On the basis of a large number of lenses of various types, we were able to calculate the amount of vitamin B<sub>1</sub> present in an individual lens.

Under our working conditions, of course, it was impossible to determine the vitamin B<sub>1</sub> content of a single lens, whether normal or not)

Furthermore, in *Ophthalmologica* (96: 219 [Jan-Feb.] 1938) I concluded

*. dass in kataraktösen Linsen das Aneurin fehlen muss, weil sie eine Brenztraubenanhäufung aufweisen. Ich habe mich damals auf diesen indirekten Nachweis beschränkt, weil der Aneurin Gehalt normalen Linsen so ausserordentlich gering ist, dass es einstweilen unmöglich erscheint, an einer einzigen Linse seinen Nachweis zu führen. Ich schätzte in meiner ersten Arbeit über diese Fragen den Aneurin Gehalt einer normalen Linse auf etwa 0,00 I γ (* that, owing to the amount of pyruvic acid in the cataractous lens, there can be no thiamine present in these lenses. I had to restrict my conclusions to this indirect way because of the extremely low thiamine content of normal lenses. This low amount precludes, for the time being, the chemical demonstration of thiamine in an individual lens. I felt justified, however, in estimating in my first paper the thiamine content of a normal lens at approximately 0.001 microgram)

From these cautious estimates Kinsey got the impression that "Veasey reported Fischer's finding of what would appear to be an incredibly small amount of thiamine in the lens, viz., 0.001 microgram. For the detection of thiamine Fischer employed Jansen's method. Jansen could detect as little as 1 microgram. It is not clear how. Fischer could detect a quantity of thiamine one-thousandth the minimum Jansen reported for pure solutions."

Kinsey wrote, furthermore, that I stated "that the results were in good agreement with those of Goudsmit and Westenbrink, who found 7 to 13 micrograms of cocarboxylase in the liver, and that 'the values for the lens are not so extremely small, if one must take into account the difference in weight between the lens and liver' Fischer would have been less misleading had he mentioned that his comparison of the weight of the lens and liver and their relative cocarboxylase content was based on the lens of an ox (2.5 Gm) and the liver of a rat (10 Gm)!"

Here, again, my statements (*Ophthalmologica*) differ greatly from what Kinsey believed to be my opinion. This will become clear if one notes what I wrote

*und steht gut im Einklang mit den Feststellungen von Goudsmit und Westenbrink, welche z.B. in der Leber 7—13γ Co-Karboxylase und nur 0,6—1,8γ Aneurin fanden, im Muskel 1,5—5γ Co-Karboxylase und nur 0,1—0,5γ Aneurin*

*Ich führe diese Zahlen an, um zu illustrieren, dass die Werte für die Linse gar nicht so extrem niedrig sind. Man denke an die Gewichtsunterschiede zwischen Linse und Leber oder Muskel und vor allem an die Unterschiede im Umfang des funktionierenden Plasmas dieser Organe (* and satisfactorily agrees with the results obtained by Goudsmit and Westenbrink, who, for instance, found in the liver 7 to 13 micrograms of cocarboxylase and only 0.6 to 1.8 micrograms of thiamine and in the muscle 1.5 to 5 micrograms of cocarboxylase but only 0.1 to 0.5 microgram of thiamine. I mention these figures for the purpose of demonstrating that the amounts found in the lens are not extraordinarily low. One must consider the differences between the weight of the lens, on the one hand, and muscle and liver, on the other, and even more the differences in the volume of functioning protoplasm in these organs.)

When Kinsey wrote "that thus the therapeutic implications (Fischer) drawn from its alleged absence in cataract are without foundation," I have to state that I never mentioned any therapeutic implications and, therefore, that implications drawn from the absence of vitamin B<sub>1</sub> in cataract are not my implications.

F. P. FISCHER, M.D., Utrecht, Netherlands

## Obituaries

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JAMES WATSON WHITE, M D

1877-1946

James Watson White was born in New Hamburg, N Y, and died in Montclair, N J, on May 15, 1946, at the age of 69 of a cerebral hemorrhage, after an illness of five days. He was the son of Richard Watson White and Sarah Celina Myers White. After receiving his preliminary education at Mount Beacon Military Academy, at Beacon, N Y, he taught school in his native Dutchess County for five years before attending Albany Medical College, from which he received his degree in medicine in 1905. He then spent eight years in general practice in New York before specializing in the diseases of the eye. In 1914 he began an association with the late Dr Alexander Duane, which continued until the latter's death, in 1926. It was through Dr Duane's stimulus that he became interested in "the anomalies of the extraocular muscles," a field to which he devoted a greater part of his time. During the last fifteen years his practice was largely limited to consultations and surgical treatment in this phase of ophthalmology. Through his teachings and writings he became widely known, and his students came from far and near to learn from him the intricacies of this complex subject. He was an expert diagnostician, with a practical viewpoint, and his large experience enabled him to cope with the most complicated "muscle case" in a highly satisfactory manner. His lack of showmanship, his honesty and his geniality won for him a host of loyal and devoted friends among his students. Teaching was his love, and he did it well, for he expounded in simple terms the theories and practice of his preceptor. He did more than any one man to popularize the teachings of Duane, and to him must be given the credit for stimulating widespread interest among ophthalmologists in the subject of ophthalmic myology. Surgical problems connected with anomalies of the inferior oblique muscle were always of great interest to him, and one of his earliest articles was entitled "Tenotomy of the Inferior Oblique Muscle" (*New York State J Med* 20: 156, 1920). In line with this work, he recently proposed that the effect of recession of the insertion of the inferior oblique muscle could be better gaged (*Surgery of Inferior Oblique at or Near the Insertion, Am J Ophth* 26 586 [June] 1943), an operation which is now being tried out.

Dr White had been on the staff of the New York Post-Graduate Medical School and Hospital of Columbia University since 1919. He became associate professor of clinical ophthalmology in 1934 and remained in that position until 1939, when he was made professor of clinical ophthalmology and executive officer of the department of

ophthalmology Although he was beyond the age of retirement, owing to the exigencies of the war, he consented to continue to serve in this capacity

During his career in ophthalmology he served on the staff of the New York Eye and Ear Infirmary, was chief of clinic and instructor of



JAMES WATSON WHITE, M D  
1877-1946

ophthalmology in the Medical Department of Columbia University and was one of the attending surgeons at the Herman Knapp Memorial Hospital He resigned his surgeonship at the last institution in 1933 to allow himself more time for his teaching At the time of his death he

was consultant in ophthalmology to the Roosevelt Hospital, New York, the Mountainside Hospital, Montclair, N J ; the Essex County Hospital for Contagious Diseases, Belleville, N J , the Newark Eye and Ear Infirmary, Newark, N J , and the Brooklyn Eye and Ear Hospital, Brooklyn

He was a member of the American Medical Association, the New York State and County Medical Society, the American Ophthalmological Society, the American Academy of Ophthalmology and Oto-Laryngology, the Orange Clinical Society, Orange, N J , the New York Ophthalmological Society, and the New York Academy of Medicine, being chairman of its Section of Ophthalmology in 1938-1939

He was an enthusiastic bass fisherman, whose skill at casting was the envy of all his companions. As a bridge player he was a keen competitor, and on the dancing floor he was thoroughly at home, so it can be seen that he was an all around man, whose love of ophthalmology did not limit his outside activities

By those of us who knew him well his memory is cherished, not only because of his professional attainments, but also because of his lovable nature. He was a considerate and true friend, with a kindly heart, whose joviality and good fellowship endeared him to all

He is survived by his widow, Margaret McClellan White, a daughter, Betty White, and a sister, Mary D White

JOHN H DUNNINGTON, M D

# Abstracts from Current Literature

EDITED BY DR WILLIAM ZENTMAYER

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## General Diseases

SJOGREN'S SYNDROME, ESPECIALLY ITS NON-OCULAR FEATURES F P WEBER, Brit J Ophth 29 299 (June) 1945

The Sjogren syndrome in its complete form includes keratoconjunctivitis sicca, xerostomia, rhinitis sicca, pharyngitis sicca and laryngitis sicca. It is, however, far more often incomplete. Weber reports several cases and discusses certain points in differential diagnosis. An abstract of the author's summary and conclusions follows.

An endeavor has been made to show of what great value Sjogren's ophthalmologic writing is for departments of medicine not especially connected with the eyes. Sjogren's syndrome is one of a group of syndromes or diseases especially affecting the female sex, including exophthalmic goiter, lymphadenoid goiter, so-called lipodystrophia progressiva superior, idiopathic hypochromic microcytic and simple achlorhydric anemias and perhaps ulcerative colitis. According to Joll, there are 9 women to 1 man in England with exophthalmic goiter. The greatest incidence occurs in the third decade of life. In Continental countries the proportion of men is higher. Lymphadenoid goiter is little known on the Continent, but a number of cases have been seen in England by Joll. Though the etiologic agent in Sjogren's syndrome, or disease, has not been discovered, it appears not to be an avitaminosis, but rather, to be of a chronic inflammatory nature and mainly to affect females, usually at or after the climacteric. Its manifold and generalized manifestations, especially in regard to the saliva and the tear- and sweat-producing glands and the glands of the gastrointestinal canal, can, Weber thinks, be explained only by a derangement of the vegetative nervous system, sometimes connected, perhaps, with structural or functional changes in the female sexual system. There may be a neuropathic predisposition.

W ZENTMAYER

## Injuries

INJURIES TO THE EYES OR TO THE INTRA-CRANIAL VISUAL PATHS IN AIR RAID CASUALTIES ADMITTED TO HOSPITAL P M BLAKE, Brit J Ophth 29 1 (Jan) 1945

Of 8,833 persons exposed to risk within 100 feet (30 meters) of the explosion in 480 high explosive bomb incidents, 0.75 per cent were admitted to the hospital with injuries to the eyes or to the visual paths. In terms of all persons with nonfatal injuries who were treated as inpatients, the proportion with injuries to the eyes or to the visual pathways was 9.6 per cent.

Forty-four per cent of the "eye" casualties lost the sight of one or both eyes or suffered impairment of vision (i e, 0 33 per cent of persons exposed to risk, or 4 2 per cent of casualties admitted to the hospital with injuries of all types). About 80 per cent of the "eye" casualties were injured by flying debris (0 18 per cent of persons exposed to risk and 2 3 per cent of casualties treated in the hospital suffered loss or impairment of vision as a result of such injuries). The proportion of direct injuries to the eye caused by flying debris was higher in parachute mine incidents than in explosions due to smaller bombs. The direct impact of the blast wave did not cause any injuries to the eyes in this series of casualties. Besides the patients with injuries to the eyeball, 15 per cent suffered from ocular injury or injuries to the intracranial visual paths as a result of fracture of the vault of the skull or of the orbital bones.

W ZENTMAYER

CATARACT PRODUCED BY ELECTRIC CURRENT E CAMPOS, *Rev brasil de oftal* 3:21 (Sept) 1944

Notwithstanding the widespread use of electricity in industry and in the home, only a few cases of cataract produced by electric current have been reported.

According to Bellows and Chinn, up to 1941 about 80 such cases had been described in the literature. Campos describes 2 more cases, observed in the service of Dr Joaquim Vidal, of Rio de Janeiro. A third case is described in detail. The patient, a man aged 61, when working with a 1575 volt transformer of 22 amperes for a current of 220 kilowatt, 110 volt current, inadvertently touched a live wire and received a shock, falling unconscious, with his forehead pressed to the wire. He remained unconscious for three hours, but after a few days' treatment he recovered almost completely. He noted, however, progressive decrease in vision, beginning in the left eye and then appearing in the right eye. Two months before examination he became totally blind.

Examination showed slight ectropion of the lower lids, with slightly everted lacrimal puncta. There were no corneal cicatrices. Extrinsic motility was normal. The pupils reacted well to light and in convergence. Complete bilateral cataract of a whitish gray color was noted. Light perception and projection were good. Operation was performed.

The author discusses various theories presented in the literature regarding the pathogenesis of cataract due to electric current, none of which are entirely satisfactory. The question is still open to discussion.

M E ALVARO

RESULTS OF SURGICAL AND CONSERVATIVE TREATMENT OF PERFORATING WOUNDS OF THE EYE F YUSEFOVA, *Vestnik oftal* 23:24, 1944

Yusefova applied combined surgical and conservative treatment to infected wounds, in both industrial and military injuries of the eye. The physicochemical part consisted in galvanocautery of the lips of the wounds and the use of sulfanilamide powder and the surgical measure in use of a conjunctival flap, according to the Kunt method.



For very serious wounds protein therapy and intravenous injections of 40 per cent methenamine were also employed

One hundred and forty cases (with no intraocular foreign bodies) were analyzed. In 70 of these cases the aforementioned method was used, in the others only conservative treatment was applied—application of drops or ointment (with removal of the prolapsed tissues). In the two groups the injury was of about the same seriousness, infection set in in about half of the cases in either group.

In summing up the results, Yusefova concludes that combined surgical and conservative treatment of severe perforating wounds of the eyeball has decreased the number of enucleations from 20 to 8.6 per cent and that visual acuity was brought up to nearly twice that obtained in cases in which the conservative treatment only was used.

The results were better the earlier after the injury the treatment was started.

O SITCHEVSKA

### Lacrimal Apparatus

HEMORRHAGE COMPLICATING DACRYOCYSTORHINOSTOMY. ITS PROPHYLAXIS AND TREATMENT. M. LORENTA BUESA, Arch. Soc. oftal. hispano-am. 4:48 (Jan.-Feb.) 1944.

Hemorrhage during and after the operation is fully discussed. The author gives his views and those of many European authorities. He reports 39 cases of his own in which hemorrhages occurred. He comes to the following conclusions: Hemorrhage is the most dreaded complication of the operation, comparable to infection following cataract extraction. The best means of avoiding hemorrhage is preoperative estimation of the bleeding and coagulation times and deferment of operation until these factors are normal. The trephining of the bone must be done as far anterior and as high as possible, to avoid the erectile zone of the turbinate process and the ethmoid cells, the nasal mucous membrane must be completely sutured. Use of the diathermy knife for the incision is convenient. The postoperative treatment of serious hemorrhages from the nasal mucous membrane generally fails. Prophylaxis should be observed.

H. F. CARRASQUILLO

### Neurology

POLYCYTHEMIA AS A NEUROSURGICAL PROBLEM. J. H. DREW and F. C. GRANT, Arch. Neurol. & Psychiat. 54:25 (July) 1945.

From an extensive review of the literature, which is well summarized in the article, the authors found reports of 17 cases of polycythemia in which the optic disks showed changes which might be considered as papilledema, or choked disk. They conclude that the occurrence of a true expanding intracranial mass lesion with polycythemia is rare but that the incident occurrence of papilledema and polycythemia is somewhat more common, but not so frequent an association as casual comments in the literature would lead one to suspect. They state that polycythemia with papilledema must be considered as a possible diagnostic and operative problem for the neurosurgeon.

S. R. IRVINE

ACUTE CORTICAL BLINDNESS WITH RECOVERY REPORT OF A CASE  
J C YASKIN and E B SPAETH, Arch Neurol & Psychiat 54:70  
(July) 1945

Because most cases of cortical blindness terminate fatally, the authors report a case deemed unusual because of its recovery. The patient became completely blind after evidence of subarachnoid hemorrhage. The neurologic abnormalities included a rigid neck and a bilateral Kernig sign, there were no other localizing signs. The pupils were large, round and central and reacted promptly to light and consensually. The fundi showed a moderate degree of arterial hypertension, with one small hemorrhage just over the macula of the right eye. In the two weeks following the patient's admission to the hospital, he gradually recovered from the glomerulonephritis and had a satisfactory return of eyesight, without any changes in the retinas.

It was felt that this man had bilateral cortical blindness. Considering the sudden onset, the lesion was probably due to a disturbance of both posterior cerebral arteries or, more likely, of the basilar artery at its bifurcation into the two posterior cerebral arteries. In view of the spontaneous subarachnoid hemorrhage, a rupture of a small aneurysm was deemed a likely process, although embolism could not be definitely ruled out.

S R IRVINE

LOCALIZING VALUE OF TEMPORAL CRESCENT DEFECTS IN THE VISUAL  
FIELDS H SHENKIN and I LEOPOLD, Arch Neurol & Psychiat  
54:97 (Aug) 1945

Five cases are presented in which unocular crescent defects in the visual field were due to verified cerebral tumors involving the supragenicate pathways. These cases emphasize the fact that careful perimetric studies may reveal a defect in one unpaired portion of the visual field, i.e., the temporal crescent, which is of practical importance to the neurologist and the neurosurgeon. A unocular crescent defect would indicate the laterality and general area involved by a tumor or other pathologic process.

No exact anatomic information may be derived from these cases. The position of the tumor itself may not tell the entire story, for cerebral tumors produce edema and other distant reactive phenomena which may also cause disturbances in the fields of vision. However, in all these 5 cases the supragenicate pathways and, more definitely, the ventromedial portion of the radiations in the parietal, temporo-parietal and parieto-occipital areas were involved.

One case particularly demonstrates the advance from a unilateral crescent cut to bilateral involvement of the field toward a homonymous hemianopsia. Other authors have previously noted that, irrespective of the location of the lesion in the optic radiation, homonymous anopsias usually begin in the periphery and advance toward the center. This brings out the importance of the temporal crescent defect as an early localizing sign.

S R IRVINE

MULTIPLE SCLEROSIS WITH LATE ONSET OF SYMPTOMS A P FRIEDMAN and C DAVISON, *Arch Neurol & Psychiat* 54 348 (Nov-Dec ) 1945

The authors stress the fact that the most important single factor in the diagnosis of multiple sclerosis in the latter years of life is the awareness that onset of symptoms is not infrequent after the age of 40

In a series of 310 patients with multiple sclerosis admitted to the Montefiore Hospital, 41 (13 per cent) had the onset of symptoms after the age of 40 Of 42 patients with multiple sclerosis on whom autopsies were performed at this hospital, 9 (21 per cent) had onset of the disease during or after the fifth decade of life

R S IRVINE

LOCALIZING VALUE OF VERTICAL NYSTAGMUS F H O'BRIEN and M B BENDER, *Arch Neurol & Psychiat* 54. 378 (Nov-Dec ) 1945

A typical case of thrombosis of the anterior spinal artery of the medulla is reported in which vertical nystagmus was observed

The localizing value of vertical nystagmus is discussed, and it is concluded that vertical nystagmus per se is of little localizing value except so far as clinical experience has shown it to be sometimes seen in cases of disease of the brain stem

S R IRVINE

UNILATERAL INTERNAL OPHTHALMOPLÉGIA SOLE CLINICAL SIGN IN PATIENT WITH SYPHILITIC MENINGITIS M A SELIGS and G F JOSEPH, *Arch Neurol & Psychiat* 54 389 (Nov-Dec ) 1945

Isolated unilateral ophthalmoplegia may be the only clinical sign in a patient with syphilitic meningitis

A case history illustrating such an occurrence is presented Syphilis obviously was the specific etiologic agent in this case However, the pathogenesis of the ophthalmoplegia is not entirely clear, since the precise anatomic site of the lesion may be nuclear, basilar, radicular or of the peripheral neuron (including the ciliary ganglion and the postganglionic fibers) No anatomicopathologic study was possible in this case However, certain deductions which lie within the realm of clinical diagnosis are forthcoming An ocular lesion (ciliary ganglion and iris) is ruled out by the demonstration of a normal pupillary response following the instillation of a miotic drug (2 drops of a 0.25 per cent solution of physostigmine salicylate was sufficient to produce miosis within about twenty minutes) Examination with the slit lamp revealed a normal iris A basilar lesion (meningeal exudate) appears unlikely in view of the absence of other neurologic signs, particularly external ophthalmoplegia and ptosis A nuclear or radicular lesion, therefore, seems the most probable, the pathologic process being either vascular or due to primary syphilitic involvement of one of the Edinger-Westphal nuclei

S R IRVINE

### Parasites

ONCHOCERCIASIS J G SCOTT, *Am J Ophth* 28:624 (June) 1945

Scott found the following ocular complications in 342 Cameroon soldiers, all of whom were assumed to be infected with *Onchoceia punctate* keratitis, 61 cases, punctate keratitis with iridocyclitis, 27 cases, and presence of microfilarias in the aqueous of otherwise unaffected eyes, 16 cases. Retrobulbar neuritis, atrophy of the optic nerve and choroiditis occurred rarely.

The microfilarias of *Onchocerca volvulus* were the most common (if not the only) microfilarias to enter the anterior chamber. Their presence was well tolerated. The cause of complications was a toxin (probably filarial, possibly microfilarial). The common occurrence of nonencapsulated filarias (*O. volvulus*) is postulated.

W ZENTMAYER

### Retina and Optic Nerve

DOUBLE THROMBOSIS OF THE CENTRAL VEIN OF THE RETINA F CANELLA, *Arch Soc oftal hispano-am* 5.164 (March) 1945

A case of this rare condition is reported. The author found only 15 similar cases in the literature.

The patient was a white man aged 25. Previous to the onset of the condition the patient had a cold, which was followed by a severe headache, lasting several days. One morning, on awakening, he could not see objects, and his legs were so weak that he could not walk. Physical examination revealed left hemiplegia and aortitis, and observation of the fundi showed a typical picture of bilateral thrombosis of the central vein.

The blood pressure was 230 systolic and 130 diastolic, and the clinical laboratory examination showed the presence of nephritis complicating the hypertensive state. Serologic reactions were negative for syphilis.

H F CARRASQUILLO

### Uvea

THE TREATMENT OF NONSPECIFIC UVEITIS WITH PENICILLIN S R IRVINE, F MAURY, J SCHULTZ, P THYGESON AND A UNSWORTH, *Am J Ophth* 28:852 (Aug) 1945

Fifty-six patients with anterior and posterior nonspecific uveitis were treated with penicillin by intramuscular injection. Eight additional patients with anterior uveitis were treated with penicillin iontophoresis.

Only in acute anterior uveitis (iridocyclitis) was significant improvement noted during or after the period of treatment. This improvement appeared to be no greater than would be expected with the use of ordinary therapeutic agents, such as atropine, heat and foreign protein.

These observations suggest that penicillin-sensitive bacteria are not ordinarily concerned in the causation of nonspecific uveitis.

W S REESE

# Society Transactions

EDITED BY DR W L BENEDICT

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NEW YORK ACADEMY OF MEDICINE, SECTION OF OPHTHALMOLOGY

Rudolph Aebli, M D, *Chairman*

Truman L Boyes, M D, *Secretary*

Jan 21, 1946

## Management of Vertical Deviation DR HAROLD W BROWN

The successful management of vertical deviation depends largely on accurate diagnosis and proper evaluation of the primary and secondary deviations. A review of the anatomic off-axis pull of the elevators and depressors shows that the oblique muscles exert their maximum vertical action when the eye is directed toward the nasal field and the superior and inferior rectus muscles when the eye is directed toward the temporal field. It will also be evident that in binocular movements an elevator or a depressor of one eye will function as a "yoke" muscle with one of the other eye, for example, elevation in the "eyes right" position is accomplished by action of the left inferior oblique muscle with its yoke muscle, the right superior rectus muscle.

The primary deviation represents the underaction of the paretic muscle, the secondary deviation, the overaction of the yoke muscle, and the secondary contracture, the overaction of the direct antagonist.

When the deviation is small and comitant, correction with prisms is indicated. A noncomitant primary deviation is corrected surgically by shortening the paretic muscle, a secondary deviation, by tenotomy or recession of the yoke muscle, a secondary contracture, by a weakening operation on the direct antagonist, and mixed types, by a combination of these operations, depending on the state of the secondary deviations and contractures.

## Hemifacial Spasm. Report of Two Cases DR DAN M GORDON

This article will appear in full in a later issue of the ARCHIVES

### DISCUSSION

DR BRONSON SANDS RAY The operative procedure employed in the first case described by Dr Gordon provided interesting observations, and I shall describe the procedure as it took place.

Local anesthesia was employed, and an incision was made in the right preauricular region along the anterior margin of the parotid gland. Except for the lowest branches of the facial nerve, supplying the platysma and the muscles of the chin and lower lip, all branches were carefully isolated at their point of emergence from the parotid gland. In all, there were six branches, the four uppermost ones being the smallest.

To begin with, each of the six branches was divided halfway through, and then the drapes were removed so that the facial motion could be more accurately determined. It was seen that the major spasms had disappeared and that there still remained fair voluntary motility in the facial muscles. The fact that a little spasm persisted in the orbicularis oculi led me to cut more fibers, therefore two of the upper four fibers were completely divided, and the larger, lower two, fibers were completely divided. The incision into the nerves was made in such a way that the scalpel was carried distally along the course of the fibers for a short distance and then turned outward, thus cutting a "slip" in the nerve trunk. The "slip" was then tied at its base with a fine silk ligature, the procedure designed to prevent regeneration of these fibers.

The immediate end result of the operation has been highly satisfactory in that the patient has virtually no spasm about the eye or the upper portion of the face. At the same time, the palpebral fissures are equal, there is moderate wrinkling of the brow, the eyes blink evenly, and there is enough retained voluntary motion at the angle of the mouth to prevent unsightly deformity. Final evaluation, of course, will require several months' observation. It is now five months since operation, and there has been no evidence of recurrence of the spasm.

**Glaucoma in a Premature Infant: Report of a Case** DR DAVID  
WEXLER and DR ABRAHAM L KORNZWEIG

This article will appear in full in a later issue of the ARCHIVES

DISCUSSION

DR A L KORNZWEIG "Buphthalmos" is an old term which is not sufficiently descriptive of congenital glaucoma. It means "ox eye" and has been used indiscriminately for such conditions as megalocornea, congenital glaucoma, high myopia and other enlargements of the eye. The term "congenital hydrophthalmos" is much better because it describes the basic pathologic process and is more in line with the terminology used for similar pathologic processes, such as hydrocephalus, in which there is interference with the circulation of aqueous or cerebrospinal fluid. Since an interference with the circulation of the aqueous is the basic pathologic condition in all cases of congenital glaucoma, the term "congenital hydrophthalmos" is a much more acceptable one.

This condition differs from high myopia in several important respects. In cases of hydrophthalmos there is uniform thinning of the coats of the eyeball, especially the sclera and the cornea, but the coats are thickest around the posterior pole. On the other hand, in cases of high myopia, though there is a uniform thinning of all the fibrous coats of the eye, it is greatest posteriorly, around the posterior pole.

The prime factor in all cases of congenital hydrophthalmos is the interference with the drainage of the aqueous at the angle of the anterior chamber. All pathologists are agreed on this fact, among them Gross, Horner, Rabb, Landolt, Seefelder, Parsons, Siegrist and Lagrange. This disturbance may be caused by the following anomalies: (1) persistent meshwork of mesoderm in the angle, (2) poor development or absence of Schlemm's canal, (3) posteriorly placed Schlemm's canal.

(4) rudimentary development of the scleral spur, (5) peripheral anterior synechias and (6) persistent iris process

Consanguinity does not appear to be of importance. Of 28 cases, the parents were related in only 3, and in 16 other cases there was no relationship between the parents.

The hyaline membrane, present in this case, is not the same as Descemet's membrane. It takes a different stain, a faint lavender, whereas Descemet's membrane can hardly be distinguished from corneal stroma. Collagen is produced by the mesodermal tissue in the cornea and in the sclera. In the cornea this collagen is transparent, and in the sclera it is opaque. The reason for this difference is probably chemical but is not actually known. It is possible for the mesodermal tissue in the anterior chamber to produce a collagenous substance which will form a hyaline membrane. The exciting cause may be increased intraocular pressure, toxemia or a local inflammatory process or possibly a combination of several factors.

### Operation for Oxycephaly with Exophthalmos DR JOSEPH E J KING

Microcephaly and mongolism, which have no relationship to oxycephaly, are excluded from this discussion.

In all cases of oxycephaly the sutures may be closed, or fixed, at an early period in life, causing various types of malformation of the skull. The skull may become tower-like (*Turmschadel*) or wedge shaped. The suture lines fuse and close tightly and are obliterated before complete closure of the anterior fontanel. This process—*cranios-tosis*—prevents proper development of the skull and brain. It is well known that the growth of the brain takes place at a rapid rate in the early years, and in so doing it exerts tremendous intracranial pressure in all directions. The closed skull gives way before this pressure at the points of least resistance, and this is usually more noticeable at the site of the closing, or recently closed, anterior fontanel. The fontanel is the last part of the suture line to close, and this thin portion of the skull is pushed out, with the resulting peculiar pointed area. The skull is misshapen and distorted, with the most prominent and bulging portion at the site of the fontanel, thus "oxy," meaning sharp, and "cephalus," meaning "head." The head may become elongated and scaphoid and yet have the most prominent protuberance at the same time.

It is not uncommon to see persons with queerly shaped heads who have normal physical and mental capacities, owing to arrest of the condition. On the other hand, oxycephalic persons may never attain adulthood. Why? The simple answer is that premature closure of the suture line prevents the intracranial space from keeping pace with the actual growth of the brain and its coverings. In other words, the brain outgrows its case, and vital functions are slowed and finally cease.

Continuation of growth of the brain in such cramped quarters results in certain symptoms and signs: (1) headaches, which may occur at an early age and not be recognized, (2) irritability and mental dulness, (3) characteristic convoluted markings of the skull, resembling billowy clouds, as well as pronounced thinning of the skull, with no, or barely distinguishable, suture lines, (4) thinning of the dura, at times almost to the thinness of cellophane, (5) unusual and abnormal

irregularities of the skull, involving most frequently and most prominently the site of the anterior fontanel, (6) tremendous increase of intracranial pressure, as shown by measurement of the intraventricular pressure (400 mm or more), and extreme diminution in the size of the ventricles (ventriculograms), (7) conspicuous bilateral papilledema, followed by atrophy, with resultant failing vision and blindness, (8) noticeable bilateral protrusion of the eyeballs and edema, or thickening of the lids, which may be so prolonged and extreme that loss of vision results, as in cases of exophthalmos associated with arteriovenous fistula or progressive exophthalmos accompanying thyroid disease, (9) generalized convulsions. If the condition is not arrested, it progresses gradually, and death ensues.

All these changes result from the slow, progressive, pronounced increase of intracranial pressure against slowly retreating, but non-elastic, walls of the cranial cavity.

Roentgenograms reveal certain similar changes, which may, however vary in degree. Characteristic is thinning of the bones of the skull in a wavy manner, with the billowy appearance of fluffy clouds. Lateral roentgenograms show this condition best, and all the bones of the cranial cavity except those forming the base present these markings. The floors of the posterior and middle fossae are depressed, with corresponding depression of the petrous pyramids and ears and depression, relative lengthening and narrowing of the sella turcica. The sella turcica is shaped like a long, deep, narrow U, instead of having the shape of an inverted  $\Omega$ . The lower jaw protrudes prominently, owing to downward displacement of the mandibular fossa. The frontal, sphenoidal and maxillary sinuses are small. The orbits are shallow and blunted and are pushed forward by pressure from within, accounting to a considerable degree for the prominence of the eyes.

The most resistant portions of the skull, which are buttressed against the oncoming pressure, are the petrous pyramids and the sphenoidal ridges. Therefore, hearing is not impaired to the same extent as vision, nor is the maxilla displaced forward like the mandible.

In 1936 I was confronted with such a case of oxycephaly. Search of the literature failed to reveal an operative procedure which would provide adequate relief. In my endeavor to find a solution, my thought continually went back to the basic fact, i.e., that the intracranial space was too small to allow of proper growth and expansion of the brain. Therefore the question arose: How can the cranial cavity be enlarged sufficiently and symmetrically without damage to the brain and its coverings? The problem was solved by the operation which will be described, and which was performed for the first time on Nov. 10, 1936 and presented as a preliminary report (*Oxycephaly: New Operation and Its Results [Preliminary Report]*, *ARCH. NEUROL. & PSYCHIAT.* 40:1205 [Dec.] 1938). The patient, a boy 8 years old, could not distinguish persons standing at the foot of his bed. Now, nine years later, he is working as a shipping clerk, in Nova Scotia. So far as can be determined, he is normal, probably somewhat short in stature, but with good muscles.



## DISCUSSION

**DR BRONSON SANDS RAY** I have had no experience with this operation. I have only watched, with great admiration, Dr King's reports. The few patients who have been presented to me for Dr King's operation have either had mongolism or microcephaly, and, as he pointed out in his opening remarks, such patients are not suitable for operation.

I should like to ask Dr King whether he can account for the apparent subsidence of exophthalmos after the operation and whether he feels it is based on the diminution of venous engorgement. I should also like to ask whether he leaves periosteum on the fragments of bone and whether he is careful to leave these segments attached to the dura.

**CAPT ARTHUR ALEXANDER KNAPP (MC), USNR** I had the pleasure of seeing the youngster from Nova Scotia before and shortly after Dr King's excellent operation. As I recall, prior to operation the child had moderate to pronounced atrophy of both optic nerves, with no papilledema. Shortly after the operation, both optic nerves were pink, and vision had improved greatly. I do not remember the precise visual acuity.

**DR JOSEPH E J KING** I was careful, in turning the soft parts down, to push the periosteum off the skull. I leave the periosteum on the segments of bone, and prefer not to knock them off the dura. They are lightly attached and very slippery, and if they wiggle off I put them back in place and close them in, and all is well. Both the dura and the pericranium are osteogenic, and the segments of skull are between the two. The fact remains that they unite and the skull becomes reformed. This is nothing new. Cushing, years ago, took out a bone flap in a case of pseudotumor and left it out, and complete regeneration occurred. In numerous cases of massive osteomyelitis of the skull the defects never have to be filled with a graft. In every case in which this operation is done, both in children and in adults, if the pericranium is stripped off with the scalp flap, the infected bone dissected out and the pericranium replaced against the dura, the patient will be all right, and the defect will close. Furstenburg, of Ann Arbor, has emphasized that, time and again. It is not necessary to fill in the defect in these cases. In cases of abscess of the brain, in which the dura and pericranium are destroyed, the defect never fills in. If in cases of compound fracture of the skull the pericranium is stripped off and some of the dura is excised, the defect will not close completely, but if pericranium is put back against the dura bone will reform. I am sure Dr Ray is acquainted with Dr Naffziger's famous case of the ash tray. His patient was an old woman with a lump on her head which stuck out like a devil's horn, and she had the same kind of lump on the inside of her skull, both osteomas. He took out a piece of bone and kept it on his desk for an ash tray. One day he took the piece of dead bone which he had used for an ash tray, ground it down inside and outside, bored holes in it and used it as a graft to fill the defect, and it took. I have transplanted a piece of skull from the morgue, and it took. If a piece of dead bone will take, a piece of live bone should

**Choroideremia** **DR BENJAMIN ESTERMAN and DR R TOWNLEY PATON**

This article will appear in full in a later issue of the ARCHIVES

## DISCUSSION

In cases of the type reported by Zorn, Parker and Fralick (Choroid-eremia, ARCH OPHTH. 6:213 [Aug] 1931), and Esterman the condition has the appearance of a genuine congenital defect. Scattered through the literature are reports of similar cases under various titles which put the matter in serious doubt. In only 1 of these cases had the patient been under observation, and in none had the tissues been studied in the laboratory, pigmentary retinitis and night blindness, with and without pigmentary changes, in the families have been reported. There are available a few cases of brothers with excellent central vision in which pictures of the fundus were made, this is to be expected when the ages are taken into consideration. Only 1 case of the condition in a female has been reported, but this speaks as strongly against a congenital defect as it does for inherited abiotrophy. Dr Falls is studying the family in the case of Parker and Fralick and reports that the mother has advanced atrophy of the choroid with sclerosis of its vessels and that a nephew, aged 6 years, shows changes in the fundus which suggest that he will later have the same type of fundus as the uncle. Except for the cases of Cowgill and Connor, all the rest could be instances of abiotrophy beginning in early life and reaching a standstill, with central vision corresponding to the amount of choroidal tissue in the macular area.

One of the cases presented here supports Dr Verhoeff's contention that a somewhat similar picture of the fundus accompanies retinitis pigmentosa, with an overgrowth of glial tissue, which shuts out the normal red color of the choroid. The macular area in such cases may be normal, with a white background elsewhere, but here and there in the periphery the choroid is dimly seen, proving that the background is not bared sclera. The type of case reported by Dr Paton is rare and conflicts with all present ideas of retinal physiology, but the condition cannot be confused with choroideremia. It is an advanced atrophy of the choroid, with the macular area persisting until the last. For this condition the title of progressive choroidal atrophy might be used until another, more suitable, term comes into use. I hope Dr Esterman and Dr Paton will keep their patients under observation and make a later report.

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Feb 21, 1946

**Fluorescent Colors in Tangent Screen Examination.** DR JACOB B  
FELDMAN and DR HAROLD J ABRAHAM, (by invitation)

This article will be published in a future issue of the ARCHIVES

**Complete Unilateral Ophthalmoplegia Due to Primary Carcinoma of the Sphenoidal Sinus Syndrome of the Orbital Apex and Superior Orbital Fissure Report of a Case DR I S TASSMAN**

This article will appear in full in a later issue of the ARCHIVES

DISCUSSION

DR BENJAMIN H SHUSTER My first association with this patient was when I made a routine examination of the ear, nose and throat, at which time I found nothing of interest I saw her a week later, during an episode of epistaxis There was nothing at this time to indicate anything but a local area of bleeding The nose was packed and the bleeding controlled One week later bleeding from the nose recurred, and I again saw the patient At this time there was also pronounced paralysis of the ocular muscles, however, the pupil reacted somewhat to light

Not being familiar with the designation "sphenoid fissure syndrome," I groped for an anatomic diagnosis The vestibular (caloric) test did not reveal any sign of an intracranial lesion Except for the ocular immobilization, there were no signs of mass in the orbit The presence of the pupillary reaction to light was evidence against the possibility of a lesion of the brain stem, which would have to be extensive to involve the number of nerves concerned in this case There were no systemic signs of cavernous sinus thrombosis, nor were edema and ecchymosis present, which are found with this condition The situation seemed to resolve itself into the possibility of a small hemorrhage at the apex of the orbit, incompletely compressing the nerves, or of a growth in the superior orbital sinus, encroaching slowly on the contents of the cavernous sinus, adjacent to its lateral wall This could compress the nerves and yet permit some venous blood to pass through, preventing the occurrence of edema and ecchymosis A specific request was made for roentgenograms of the orbit and sphenoid sinus The latter were misinterpreted, and the sphenoid was pronounced normal

It was decided to explore the orbit through an incision at its medial border If an erosion was found on the nasal wall, it could be followed through No such break was found, and in view of the negative report on the sphenoidal sinus no further search was made The possibility of an intracranial lesion had to be considered Shortly after the operation the roentgenograms were again studied, and the conclusion was reached that the sphenoidal sinus as well as other sinuses were involved Accordingly, it was decided to reexplore the wound, with the idea of breaking through to the sinuses, and an attempt to reach the sinuses through the nasal wall was first made

A sphenoid probe was introduced, and it was immediately found that the posterior bony wall of the sphenoidal sinus was destroyed The nose at first appeared to be normal, but after the bony covering was broken down a mass of malignant-appearing tissue was seen in the sphenoidal, ethmoidal and maxillary sinuses Microscopic study of the tissue showed that it was malignant I believe that Dr Tassman is correct in his contention that the primary growth was in the sphenoidal sinus The vague headache and the bulk of the mass present in the sphenoidal sinus pointed in that direction Those who have seen cases of malignant growths of the antrum will agree that in view of the length of time

the condition existed in this patient, the orbit would have been invaded much sooner and would not have involved the nerves alone but the entire intraorbital contents

The orbital incision employed in this case is routine for extranasal exenteration of the sinuses. It affords a satisfactory exposure of the orbit in its floor, median wall and roof

DR HENRY A SHENKIN The neurosurgeon's interest in this patient lies in the possibility of an intracranial lesion producing this syndrome, particularly a tumor of the sphenoidal ridge. Unquestionably, the outstanding point in the differential diagnosis is the fact that meningioma of the sphenoidal ridge is a slow-growing lesion, the symptoms being gradually progressive over a period of years, or at least of many months. For this reason, involvement of the external ocular muscles is rarely complete, the slowly growing lesion distorting, but not completely interrupting, the nerves passing through that region.

There may be blindness from a meningioma of the sphenoidal ridge. I believe that at least 25 per cent of patients with such a lesion have seriously impaired vision, but this is usually accompanied with primary atrophy of the optic nerve resulting from pressure by the optic nerve for a long time. Carcinoma of the sinuses may cause exophthalmos, which is also an outstanding symptom of meningioma of the sphenoidal ridge. Roentgenograms would reveal hyperostosis of the orbital roof and of the wings of the sphenoid in cases of the latter. With such exophthalmos the optic bulb would tend to be depressed, owing to exostosis of the orbital roof. Malignant growths of the sinuses are accompanied with erosion of the bones of the orbital cavity and the bones nearby.

DR I S TASSMAN Cases of this kind are unusual. This patient came to my attention for the ocular condition while she was on the medical service under treatment for vascular hypertension. As Dr Shuster pointed out, it was logical to enter the orbit on the medial aspect, so that the sinuses could be easily entered at the same time if this appeared to be indicated. Strangely, the orbital walls were found to be normal, and the nasal sinuses gave no evidences of the presence of any disease.

In spite of this, I strongly suspected trouble in the sinuses even prior to the orbital exploration, especially because of the chemosis of the conjunctiva. The possibility of a retro-orbital lesion was also considered seriously, and it was recognized that there was pressure to produce the congestion and chemosis. However, all this time there was no exophthalmos of the right eye. I believe that absence of this sign was important evidence in eliminating an intraorbital or a retro-orbital growth. Although it was recognized that the second, third and fourth cranial nerves, the ophthalmic branch of the fifth nerve and the sixth nerve were involved, the etiologic factor was obscure until the time of operation. For this reason, and because of the infrequency of reported cases, it was felt that this case should be recorded.

#### **Tendon Transplantation for Paralysis of the External Rectus Muscle.**

E SPAETH, M D,

The use of tendon transplants from the superior and inferior rectus muscles for the correction of paralytic strabismus involving the external

rectus muscle was presented by means of moving pictures. This operation is indicated only in cases in which the paralytic eye can be moved spontaneously up to the midline. In cases in which the eye remains in paralytic convergence, this procedure can accomplish no more than an ordinary recession of the internal rectus and resection of the paralytic external rectus muscle. In properly selected cases 15 to 30 degrees of external rotation has been achieved. The principles underlying the procedure are twofold. The first is a release in the paralytic convergence by the recession of the internal rectus muscle and a reduction in internal rotation ability by half through the use of the tendon transplant from the superior and inferior rectus muscles. Second, the transplant holds the eye in the "eyes front" position, or even in slight latent divergence, permitting the two oblique muscles to function more adequately as external rotators. The internal rectus muscle after recession furnishes adequate convergence for near work. The operation has its chief indication in cases in which there is acquired paralysis of the external rectus muscle, rather than in cases of congenital palsy.

#### DISCUSSION

DR LOUIS LEHRFELD. Dr Spaeth may recall my exhibit of 2 cases of Hummelsheimer operation at a conference at the Wills Eye Hospital several years ago. One of the patients presented there I saw last week at the Wills Hospital clinic. The result was excellent.

The technic differs slightly from that just shown. Instead of transplanting the sections of the tendon of the superior and inferior rectus muscles above and below the insertion of the external rectus muscle, Hummelsheimer recommends that the tendon transplants be inserted under the insertion of the external rectus muscle.

I think that the key to success of such muscle transplantations rests in firm anchoring of the transplanted tendons to their new positions. I found that this can be best accomplished with the use of silk sutures, inasmuch as they are unabsorbable.

Last year I used the Hummelsheimer technic in operation on a patient who had paralysis of the superior rectus muscle associated with ptosis. To my surprise, I not only achieved a fair result in restoring partial function of the superior rectus muscle but also obtained a reduction in the amount of ptosis.

I hope that Dr Spaeth's presentation tonight will stimulate the surgeons to resort to this method of tendon transplantation in correction of paralysis, not only of the external rectus muscle but of all ocular muscles.

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Place Palmer House, Chicago Time Oct 13-18, 1946

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President Dr Eugene M Blake, 303 Whitney Ave, New Haven, Conn

Secretary-Treasurer Dr Walter S Atkinson, 129 Clinton St, Watertown, N Y

Place San Francisco Time June 26-28, 1946

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 Place New York Time Nov 25-27, 1946

SECTIONAL

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 EYE, EAR, NOSE AND THROAT

President Dr Anthony Ambrose, 31 Lincoln Park, Newark  
 Secretary Dr William F Keim Jr, 15 Washington St, Newark 2  
 Place 91 Lincoln Park South, Newark Time 8 45 p m, second Monday of  
 each month, October to May

CENTRAL ILLINOIS SOCIETY OF OPHTHALMOLOGY AND OTOLARYNGOLOGY

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 Secretary-Treasurer Dr L Q Pang, 52 S Vineyard St, Honolulu 39  
 Place Honolulu Time Third Thursday of each month

NEW ENGLAND OPHTHALMOLOGICAL SOCIETY

President Dr Howard F Hill, 177 Main St, Waterville, Maine  
 Secretary-Treasurer Dr Merrill J King, 264 Beacon St, Boston 16  
 Place Massachusetts Eye and Ear Infirmary, 243 Charles St, Boston Time  
 8 p m, third Tuesday of each month from November to April, inclusive

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President Dr Julius A Weber, 640 Stimson Bldg, Seattle 1, Wash  
 Secretary-Treasurer Dr Barton E Peden, 301 Stimson Bldg, Seattle 1, Wash  
 Place Seattle or Tacoma, Wash Time Third Tuesday of each month except  
 June, July and August

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President Dr J Sheldon Clark, Sterling, Ill  
 Secretary-Treasurer Dr Harry R Warner, 321 W State St, Rockford, Ill  
 Place Rockford, Ill, or Janesville or Beloit, Wis Time Third Tuesday of each  
 month from October to April, inclusive

SAGINAW VALLEY ACADEMY OF OPHTHALMOLOGY AND OTOLARYNGOLOGY

President Dr A R McKinney, 330 S Washington St, Saginaw, Mich  
 Secretary-Treasurer Dr Harold H Heuser, 207 Davidson Bldg, Bay City, Mich  
 Place Saginaw or Bay City, Mich Time Second Tuesday of each month, except  
 July, August and September

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 Secretary-Treasurer Dr Kenneth Lowe, 25 W Michigan Ave, Battle Creek  
 Time Last Thursday of September, October, November, March, April and May

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 Secretary Dr J Leonard Swigert, 320 Republic Bldg, Denver  
 Place University Club, Denver Time 7 30 p m, third Saturday of each month  
 October to May, inclusive

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 Secretary Dr Russell A Sage, 23 E Ohio St, Indianapolis  
 Place French Lick Time First Wednesday in April

## IOWA ACADEMY OF OPHTHALMOLOGY AND OTO-LARYNGOLOGY

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KANSAS STATE MEDICAL SOCIETY, SECTION ON OPHTHALMOLOGY AND  
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 Secretary Dr George F Gsell, 911 Beacon Bldg, Wichita 2

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Secretary-Treasurer Dr Edley H Jones, 1301 Washington St, Vicksburg, Miss

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AND OTOLARYNGOLOGY

Chairman Dr Edmond L Cooper, 1553 Woodward Ave, Detroit 26  
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President Dr Karl C Wold, 1051 Lowry Bldg, St Paul 2  
Secretary Dr William A Kennedy, 372 St Peter St, St Paul 2  
Time Second Friday of each month from October to May

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Secretary Dr Fritz D Hurd, 309 Medical Arts Bldg, Great Falls

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THROAT SECTION

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Secretary Dr Thomas H Johnson, 30 W 59th St, New York

NORTH CAROLINA EYE, EAR, NOSE AND THROAT SOCIETY

President Dr A J Ellington, 412 S Spring St, Burlington  
Secretary Dr J A Harrill, Bowman Gray School of Medicine, Winston-Salem  
Place Hendersonville Time Sept 16-19, 1946

NORTH DAKOTA ACADEMY OF OPHTHALMOLOGY AND OTO-LARYNGOLOGY

President Dr E D Perrin, 221-5th St, Bismarck  
Secretary-Treasurer Dr M T Lampert, Minot

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President Dr Wilfred Belnap, 833 S W 11th Ave, Portland  
Secretary-Treasurer Dr C W Kuhn, 1020 S W Taylor St, Portland 5  
Place Good Samaritan Hospital, Portland Time Third Tuesday of each month

PENNSYLVANIA ACADEMY OF OPHTHALMOLOGY AND OTOLARYNGOLOGY

President Dr Thomas F Furlong Jr, 36 Parking Plaza, Ardmore  
Secretary Dr Benjamin F Souders, 143 N 6th St, Reading  
Time Last week in April

## RHODE ISLAND OPHTHALMOLOGICAL AND OTOLOGICAL SOCIETY

Acting President Dr N Darrell Harvey, 112 Waterman St, Providence  
 Secretary-Treasurer Dr Linley C Happ, 124 Waterman St, Providence  
 Place Rhode Island Medical Society, Library, Providence Time 8 30 p m,  
 second Thursday in October, December, February and April

## SOUTH CAROLINA SOCIETY OF OPHTHALMOLOGY AND OTOLARYNGOLOGY

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 Secretary-Treasurer Dr Roderick Macdonald, 330 E Main St, Rock Hill  
 Place Hendersonville, N C Time Sept 16-19, 1946

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 Secretary-Treasurer Dr Sam H Sanders, 1089 Madison Ave, Memphis

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 Secretary Dr M K McCullough, 1717 Pacific Ave, Dallas

## UTAH OPHTHALMOLOGICAL SOCIETY

President Dr E B Fairbanks, 315 Medical Arts Bldg, Salt Lake City  
 Secretary-Treasurer Dr Dean Spear, 516 Boston Bldg, Salt Lake City  
 Place University Club, Salt Lake City Time 7 00 p m, third Monday of  
 each month

## VIRGINIA SOCIETY OF OTO-LARYNGOLOGY AND OPHTHALMOLOGY

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 Secretary-Treasurer Dr Francis H McGovern, 105 S Union St, Danville

WEST VIRGINIA STATE MEDICAL ASSOCIATION, EYE, EAR, NOSE AND  
THROAT SECTION

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 Secretary Dr Welch England, 621½ Market St, Parkersburg

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## AKRON ACADEMY OF OPHTHALMOLOGY AND OTOLARYNGOLOGY

President Dr E L Mather, 39 S Main St, Akron, Ohio  
 Secretary-Treasurer Dr V C Malloy, 2d National Bank Bldg, Akron, Ohio  
 Time First Monday in January, March, May and November

## ATLANTA EYE, EAR, NOSE AND THROAT SOCIETY

President Dr B M Cline, 153 Peachtree St N E, Atlanta, Ga  
 Secretary Dr Lester A Brown, 815 Doctors Bldg, Atlanta, Ga  
 Place Academy of Medicine Time 7 30 p m, fourth Monday of each month  
 from October to May

## BALTIMORE MEDICAL SOCIETY, SECTION ON OPHTHALMOLOGY

Chairman Dr Jonas Friedenwald, 1212 Eutaw Pl, Baltimore  
 Secretary Dr Fred Reese, 330 N Charles St, Baltimore 1  
 Place Medical and Chirurgical Faculty, 1211 Cathedral St Time 8 30 p m,  
 fourth Thursday of each month from October to March

BIRMINGHAM EYE, EAR, NOSE AND THROAT CLUB

President Each member, in alphabetical order  
 Secretary Dr W Chunn Parsons, 425 Woodward Bldg, Birmingham, Ala  
 Place Tutwiler Hotel Time 6 30 p m, second Tuesday of each month, September to May, inclusive

BROOKLYN OPHTHALMOLOGICAL SOCIETY

President Dr Benjamin C Rosenthal, 140 New York Ave, Brooklyn  
 Secretary-Treasurer Dr Louis Freemark, 256 Rochester Ave, Brooklyn 13  
 Place Kings County Medical Society Bldg, 1313 Bedford Ave Time Third Thursday in February, April, May, October and December

BUFFALO OPHTHALMOLOGIC CLUB

President Dr William H Howard, 389 Linwood Ave, Buffalo 9  
 Secretary-Treasurer Dr Sheldon B Freeman, 196 Linwood Ave, Buffalo 9  
 Time Second Thursday of each month from October to May

CHATTANOOGA SOCIETY OF OPHTHALMOLOGY AND OTOLARYNGOLOGY

President Each member, in alphabetical order  
 Secretary Dr Douglas Chamberlain, Chattanooga Bank Bldg, Chattanooga, Tenn  
 Place Mountain City Club Time Second Thursday of each month from September to May

CHICAGO OPHTHALMOLOGICAL SOCIETY

President Dr W A Mann, 30 N Michigan Ave, Chicago 2  
 Secretary Dr. J R Fitzgerald, 3215 W North Ave, Chicago  
 Place Continental Hotel, 505 N Michigan Ave Time Third Monday of each month from October to May

CINCINNATI GENERAL HOSPITAL OPHTHALMOLOGY STAFF

Chairman Dr D T Vail, 441 Vine St, Cincinnati  
 Secretary Dr A A Levin, 441 Vine St, Cincinnati  
 Place Cincinnati General Hospital Time 7 45 p m, third Friday of each month except June, July and August

CLEVELAND OPHTHALMOLOGICAL CLUB

Chairman Dr M Paul Motto, Rose Bldg, Cleveland  
 Secretary Dr H H Wygand, 624 Guardian Bldg, Cleveland  
 Time Second Tuesday in October, December, February and April

COLLEGE OF PHYSICIANS, PHILADELPHIA, SECTION ON OPHTHALMOLOGY

Chairman Dr Burton Chance, 317 S 15th St, Philadelphia  
 Clerk Dr George F J Kelly, 37 S 20th St, Philadelphia  
 Time Third Thursday of every month from October to April, inclusive

COLUMBUS OPHTHALMOLOGICAL AND OTO-LARYNGOLOGICAL SOCIETY

Chairman Dr M Goldberg, 328 E State St, Columbus, Ohio  
 Secretary-Treasurer Dr W J Miller, 21 E State St, Columbus, Ohio  
 Place University Club Time 6 15 p m, first Monday of each month, from October to May, inclusive

CORPUS CHRISTI EYE, EAR, NOSE AND THROAT SOCIETY

Chairman Dr L W O Janssen, 710 Medical Professional Bldg, Corpus Christi, Texas  
 Secretary Dr F B Kelly, 519 Medical Professional Bldg, Corpus Christi, Texas  
 Time 6 30 p m, third Tuesday of each month from October to May

## DALLAS ACADEMY OF OPHTHALMOLOGY AND OTO-LARYNGOLOGY

President Dr Speight Jenkins, 1719 Pacific Ave, Dallas, Texas  
 Secretary Dr L Darrough, Dallas Medical and Surgical Clinics, Dallas, Texas  
 Place Dallas Athletic Club Time 6 30 p m, first Tuesday of each month  
 from October to June The November, January and March meetings are  
 devoted to clinical work

## DES MOINES ACADEMY OF OPHTHALMOLOGY AND OTOLARYNGOLOGY

President Dr H I McPherrin, 406-6th Ave, Des Moines, Iowa  
 Secretary-Treasurer Dr C C Jones, Bankers Trust Bldg, Des Moines, Iowa  
 Time 7 45 p m, fourth Monday of every month from September to May

## DETROIT OPHTHALMOLOGICAL CLUB

Chairman Members rotate alphabetically  
 Secretary Dr Wesley G Reid, 974 Fisher Bldg, Detroit 2  
 Place Club rooms of Wayne County Medical Society Time First Monday of  
 each month, November to April, inclusive

## DETROIT OPHTHALMOLOGICAL SOCIETY

President Dr Bruce Fralick, 201 S Main St, Ann Arbor, Mich  
 Secretary Dr William S Gonne, 619 David Whitney Bldg, Detroit 26  
 Place Club rooms of Wayne County Medical Society Time 6 30 p m, third  
 Thursday of each month from November to April, inclusive

## EASTERN NEW YORK EYE, EAR, NOSE AND THROAT ASSOCIATION

President Dr Frank C Furlong, 713 Union St, Schenectady  
 Secretary-Treasurer Dr E Martin Freund, 762 Madison Ave, Albany  
 Time Third Wednesday in October, November, March, April, May and June

## FORT WORTH EYE, EAR, NOSE AND THROAT SOCIETY

President Dr C R Lees, 602 W 10th St, Fort Worth 2, Texas  
 Secretary-Treasurer Dr Van D Rathgeber, 1305 Medical Arts Bldg, Fort  
 Worth, Texas  
 Place Medical Hall, Medical Arts Bldg Time 7 30 p m, first Friday of each  
 month except July and August

HOUSTON ACADEMY OF MEDICINE, OPHTHALMOLOGICAL AND  
OTO-LARYNGOLOGICAL SECTION

President Dr J Matt Robison, 1304 Walker Ave, Houston, Texas  
 Secretary Dr John H Barrett, 1304 Walker Ave, Houston, Texas  
 Place River Oaks Country Club Time 6 30 p m, second Thursday of each  
 month from October to June

## INDIANAPOLIS OPHTHALMOLOGICAL AND OTOLARYNGOLOGICAL SOCIETY

President Dr J Jerome Littell, 603 Hume Mansur Bldg, Indianapolis  
 Secretary Dr J Lawrence Sims, 23 E Ohio St, Indianapolis  
 Place Indianapolis Athletic Club Time 6 30 p m, second Thursday of each  
 month from November to May

## KANSAS CITY SOCIETY OF OPHTHALMOLOGY AND OTO-LARYNGOLOGY

President Dr Edgar Johnson, 906 Grand Ave, Kansas City, Mo  
 Secretary Dr W E Keith, 1103 Grand Ave, Kansas City, Mo  
 Time Third Thursday of each month from October to June The November,  
 January and March meetings are devoted to clinical work

LONG BEACH EYE, EAR, NOSE AND THROAT SOCIETY

Chairman Dr Francis Carl Hertzog, 117 E 8th St, Long Beach, Calif  
 Secretary-Treasurer Dr Robert G Thornburgh, 117 E 8th St, Long Beach, Calif  
 Place Seaside Hospital Time Last Wednesday of each month from October to May

LOS ANGELES SOCIETY OF OPHTHALMOLOGY AND OTOLARYNGOLOGY

President Dr A R Robbins, 1930 Wilshire Blvd, Los Angeles  
 Secretary-Treasurer Dr K C Brandenburg, 110 Pine Ave, Long Beach 2, Calif  
 Place Los Angeles County Medical Association Bldg, 1925 Wilshire Blvd Time  
 6 30 p m, fourth Monday of each month from September to May, inclusive

LOUISVILLE EYE AND EAR SOCIETY

President Dr Joseph S Heitger, Heyburn Bldg, Louisville, Ky  
 Secretary-Treasurer Dr J W Fish, 321 W Broadway, Louisville, Ky  
 Place Brown Hotel Time 6 30 p m, second Thursday of each month from September to May, inclusive

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Chairman Each member in alphabetical order  
 Secretary Dr James J Monohan, 31 S Jardin St, Shenandoah, Pa

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 OPHTHALMOLOGY AND OTOLARYNGOLOGY

Chairman Dr P S Constantinople, 1835 I St N W, Washington  
 Secretary Dr Frazier Williams, 1801 I St N W, Washington  
 Place 1718 M St N W Time 8 p m, third Friday of each month from October to April, inclusive

MEMPHIS SOCIETY OF OPHTHALMOLOGY AND OTOLARYNGOLOGY

Chairman Each member, in alphabetical order  
 Secretary Dr Sam H Sanders, 1089 Madison Ave, Memphis, Tenn  
 Place Eye Clinic of Memphis Eye, Ear, Nose and Throat Hospital Time 8 p m,  
 second Tuesday of each month from September to May

MILWAUKEE OTO-OPHTHALMIC SOCIETY

President Dr Ralph T Rank, 238 W Wisconsin Ave, Milwaukee  
 Secretary-Treasurer Dr Frank G Treskow, 411 E Mason St, Milwaukee 2  
 Place University Club Time 6 30 p m, fourth Tuesday of each month from October to May

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Chairman Dr H V Dutrow, 1040 Fidelity Medical Bldg, Dayton, Ohio  
 Secretary-Treasurer Dr Maitland D Place, 981 Reibold Bldg, Dayton, Ohio  
 Place Van Cleve Hotel Time 6 30 p m, first Tuesday of each month from October to June, inclusive

MONTREAL OPHTHALMOLOGICAL SOCIETY

President Dr J Rosenbaum, 1396 Ste Catherine St W, Montreal Canada  
 Secretary Dr L Tessier, 1230 St Joseph Blvd E, Montreal, Canada  
 Time Second Thursday of October, December, February and April

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Chairman Dr M M Cullom, 700 Church St, Nashville, Tenn  
 Secretary Dr R E Sullivan, 432 Doctors Bldg, Nashville 3, Tenn  
 Place James Robertson Hotel Time 6 30 p m, third Monday of each month from October to May



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President Dr W B Clark, 1012 American Bank Bldg, New Orleans  
 Secretary Dr Mercer G Lynch, 1018 Maison Blanche Bldg, New Orleans  
 Place Louisiana State University Medical Bldg Time 8 p m, second Tuesday  
 of each month from October to May

## NEW YORK ACADEMY OF MEDICINE, SECTION OF OPHTHALMOLOGY

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 Secretary Dr Milton Berliner, 57 W 57th St, New York  
 Time 8 30 p m, third Monday of every month from October to May, inclusive

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President Dr Benjamin Friedman, 6 W 77th St, New York.  
 Secretary Dr Benjamin Esterman, 983 Park Ave, New York 28  
 Place New York Academy of Medicine, 2 E 103d St Time 8 p m, first Monday  
 of each month from October to May, inclusive

## OKLAHOMA CITY ACADEMY OF OPHTHALMOLOGY AND OTOLARYNGOLOGY

President Dr S R Shaver, 117 N Broadway, Oklahoma City  
 Secretary Dr William Mussil, Medical Arts Bldg, Oklahoma City  
 Place University Hospital Time Second Tuesday of each month from Sep-  
 tember to May

OMAHA AND COUNCIL BLUFFS OPHTHALMOLOGICAL AND  
OTO-LARYNGOLOGICAL SOCIETY

President Dr A A Steinberg, 1502 Farnam St, Omaha  
 Secretary-Treasurer Dr W Howard Morrison, 1500 Medical Arts Bldg, Omaha 2  
 Place Omaha Club, 20th and Douglas Sts, Omaha Time 6 p m dinner, 7 p m  
 program, third Wednesday of each month from October to May

## PASSAIC-BERGEN OPHTHALMOLOGICAL CLUB

President Dr Thomas Sanfacon, 340 Park Ave, Paterson, N J  
 Secretary-Treasurer Dr J Averbach, 435 Clifton Ave, Clifton, N J  
 Place Paterson Eye and Ear Infirmary Time 9 p m, last Friday of every  
 month, except June, July and August

## PHILADELPHIA COUNTY MEDICAL SOCIETY, EYE SECTION

President Dr L Waller Winckler, Philadelphia  
 Secretary Dr Robert T M Donnelly, 255 S 17th St, Philadelphia  
 Time First Thursday of each month from October to May

## PITTSBURGH OPHTHALMOLOGICAL SOCIETY

President Dr Clarence F Bernatz, Park Bldg, Pittsburgh  
 Secretary Dr Robert J Billings, Park Bldg, Pittsburgh  
 Place Pittsburgh Academy of Medicine Bldg Time Fourth Monday of each  
 month, except June, July, August and September

## READING EYE, EAR, NOSE AND THROAT SOCIETY

President Dr Claude W Bankes, 212 N 6th St, Reading, Pa  
 Secretary Dr Paul C Craig, 232 N 5th St, Reading, Pa  
 Place Wyomissing Club Time 6 30 p m, third Wednesday of each month  
 from September to July

RICHMOND EYE, EAR, NOSE AND THROAT SOCIETY

President Dr Luther C Brawner, Professional Bldg, Richmond, Va  
 Secretary Dr Clifford A Folkes, Professional Bldg, Richmond, Va  
 Place Westmoreland Club Time 6 p m, second Monday of each month from  
 October to May

ROCHESTER EYE, EAR, NOSE AND THROAT SOCIETY

President Dr Frank Barber, 75 S Fitzhugh St, Rochester, N Y  
 Secretary-Treasurer Dr Charles T Sullivan, 277 Alexander St, Rochester, N Y

ST LOUIS OPHTHALMIC SOCIETY

President Dr A Lange, 3903a Olive St, St Louis  
 Secretary Dr William Klemberg, Frisco Bldg, St Louis  
 Place Oscar Johnson Institute Time Fourth Friday of each month from October  
 to April, inclusive, except December, at 8 00 p m

SAN ANTONIO OPHTHALMO-OTO-LARYNGOLOGICAL SOCIETY

President Dr Belvin Pritchett, 705 E Houston St, San Antonio 5, Texas  
 Secretary-Treasurer Lt Col John L. Matthews, AAF School of Aviation Medi-  
 cine, Randolph Field, Texas  
 Place San Antonio, Brooke General Hospital, Randolph Field or San Antonio  
 Aviation Cadet Center Time 7 p m, second Tuesday of each month from  
 October to May

SAN FRANCISCO COUNTY MEDICAL SOCIETY, SECTION ON EYE,  
 EAR, NOSE AND THROAT

Chairman Dr C B Cowan, 490 Post St, San Francisco  
 Secretary Dr D Harrington, 384 Post St, San Francisco  
 Place Society's Bldg, 2180 Washington St, San Francisco Time Fourth  
 Tuesday of every month except June, July and December

SHREVEPORT EYE, EAR, NOSE AND THROAT SOCIETY

President Dr David C Swearingen, Slattery Bldg, Shreveport, La  
 Secretary-Treasurer Dr Kenneth Jones, Medical Arts Bldg, Shreveport, La  
 Place Shreveport Charity Hospital Time 7 30 p m, first Monday of every  
 month except July, August and September

SPOKANE ACADEMY OF OPHTHALMOLOGY AND OTO-LARYNGOLOGY

President Dr Clarence A Veasey Sr, 421 W Riverside Ave, Spokane, Wash  
 Secretary Dr Clarence A Veasey, 421 W Riverside Ave, Spokane, Wash  
 Place Spokane Medical Library Time 8 p m, fourth Tuesday of each month  
 except June, July and August

SYRACUSE EYE, EAR, NOSE AND THROAT SOCIETY

President Dr A H Rubenstein, 713 E Genesee St, Syracuse, N Y.  
 Secretary-Treasurer Dr I H Blaisdell, 713 E Genesee St, Syracuse, N Y  
 Place University Club Time First Tuesday of each month except June, July  
 and August

TOLEDO EYE, EAR, NOSE AND THROAT SOCIETY

Chairman Dr W W Randolph, 1838 Parkwood Ave, Toledo 2, Ohio  
 Secretary Dr John L Roberts, 316 Michigan St, Toledo, Ohio  
 Place Toledo Club Time Each month except June, July and August

## TORONTO ACADEMY OF MEDICINE, SECTION OF OPHTHALMOLOGY

Chairman Dr R G C Kelly, 14 Lynwood Ave, Toronto 5, Canada

Secretary Dr Alfred Ellhott, 802 Medical Arts Bldg, Toronto 5, Canada

Place Academy of Medicine, 13 Queens Park Time First Monday of each month, November to April

## WASHINGTON, D C, OPHTHALMOLOGICAL SOCIETY

President Dr Harold M Downey, 1740 M St N W, Washington, D C

Secretary-Treasurer Dr Richard W Wilkinson, 1408 L St N W, Washington, D C

Place Medical Society of District of Columbia Bldg, 1718 M St N W, Washington, D C Time 7 30 p m, first Monday in November, January, March and May

## WILKES-BARRE OPHTHALMOLOGICAL SOCIETY

Chairman Each member in turn

Secretary Dr Samuel T Buckman, 70 S Franklin St, Wilkes-Barre, Pa

Place Office of chairman Time Last Tuesday of each month from October to May

# ARCHIVES OF OPHTHALMOLOGY

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## SELECTION OF COLOR VISION TESTS FOR THE ARMY AIR FORCES

*A Summary of Studies Made at the Army Air Forces School of Aviation Medicine*

LOUISE L SLOAN, Ph D \*  
RANDOLPH FIELD, TEXAS

SINCE the establishment of the Research Section of the Army Air Forces School of Aviation Medicine in December 1941, research on color vision has been one of the major projects of the department of ophthalmology. The primary purpose of these studies was to select tests for deficiency in red-green color vision which would be suitable for use in the selection of air force personnel. The material covered in this review is based principally on investigations carried out at the Army Air Forces School of Aviation Medicine between June 1942 and June 1945.

At the time these studies were initiated, four tests of color vision were authorized for use in the Army Air Forces: two basic tests and two adjunct tests<sup>1</sup>. The basic tests were the Ishihara test (eighth edition) and the American Optical Company Pseudo-Isochromatic Plates. The criterion of passing for both tests was that not more than 25 per cent of the plates be read incorrectly. It is not clear whether the decision to allow errors on a small number of plates was made with the idea that it would qualify men with only mild defects in color vision or because it was recognized that subjects with normal color vision read some of the charts incorrectly. A study of the adequacy

From the Army Air Forces School of Aviation Medicine

\* On leave of absence from the Wilmer Ophthalmological Institute of the Johns Hopkins University and Hospital, 1942-1945

1 Wallace, S R, Jr, and Rowland, L S. The Present Status of Color Vision Testing in the Army Air Forces, Report on File at Research Library, AAF School of Aviation Medicine, Randolph Field, Texas, March 29, 1944. Because of Civil Service Regulations, the second author's married name was used in the reports from the School of Aviation Medicine. Articles in journals are signed "Louise L Sloan."

2 Rowland, L S, and Heagan, F V. Frequency of Color Deficiency Among Air Corps Cadets, AAF School of Aviation Medicine, Project no 314, Report no 1, Randolph Field, Texas, Aug 31, 1944

of the basic tests as actually administered in the Army Air Forces<sup>2</sup> revealed that approximately one-half the subjects with deficient color vision remained undetected in repeated examinations. A similar study of the efficiency of the same tests as administered in the Navy<sup>3</sup> revealed the same percentage of candidates undetected with deficiency in color vision and revealed essentially the same factors to be responsible for failure to detect the defect.

The two adjunct tests authorized by the regulations were the Holmgren wool test and the School of Aviation Medicine lantern test. Ability to pass these tests was used to qualify men as "color safe" under certain conditions. Qualification for certain aircrew tasks was also made on the basis of the subject's ability to "distinguish and identify without confusion the color of an object, substance, material, or light that is uniformly colored a vivid red, and of an object, substance, material, or light that is uniformly colored a vivid green." The regulation gave no further information, consequently, it was left to the individual examiner to select a test and devise a method of scoring it so as to distinguish between those who did and those who did not meet this criterion. The wording of the regulation suggests, however, that its intention was to disqualify only those with complete red-green vision deficiency.

It is obvious that these color vision requirements are completely arbitrary. An analysis of available information regarding the color discriminations required of air crew, combat crew and ground crew members was needed to determine first whether normal color vision is essential for all such tasks. If not, and if a certain degree of deficiency in color vision can be permitted for certain tasks, then it is obvious that there is need not only for tests to distinguish subjects with normal from those with deficient color vision but also for tests which will measure the degree of deficiency.

The logical requirements for a thorough study of this problem can be outlined as follows:

(a) A "job analysis" to determine the type of color discrimination required of aircrew personnel, for example, pilots, navigators, bombardiers, gunners and radio operators, and ground crew personnel, for example, control tower operators, engineers and truck drivers.

(b) An evaluation of the already available tests for red-green color discrimination from the following points of view: (1) suitability as a screening test to distinguish between normal and deficient color vision or as a quantitative test for degree of defect, (2) reproducibility of

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<sup>3</sup> Farnsworth, D., and Reed, J. D. A Survey of Methods Used in Administering Pseudo-Isochromatic Test Plates for Color Vision, Medical Research Laboratory, New London, Conn., Color Vision Report no. 3, Nov. 6, 1943.

the results in successive tests with respect to classification as normal or deficient color discrimination or with respect to degree of defect if color vision is deficient, (3) time required for administration and scoring of test, (4) possibility that applicants with deficient color vision might be coached to pass the test, (5) probability that scores on the test will be related to performance in color discriminations required in practice

(c) The development and standardization of new tests if those already available are inadequate

(d) Validation studies of the relationship between scores on various selected tests and performance in field tests simulating actual situations

(e) From the results obtained in (d), selection of the most satisfactory test or tests and adoption of critical qualifying scores for various jobs

The various lines of investigation summarized here were not actually carried out in the exact order given but were conducted more or less simultaneously, since it was necessary to adapt the conditions of the study to the facilities available and to study different aspects of the problem at the time that the particular tests, subjects, etc., were available

#### ANALYSIS OF COLOR DISCRIMINATIONS REQUIRED OF AIRCREW PERSONNEL

The various types of color discrimination which may be of importance for aircrew personnel may be summarized as follows

1 *Identification of Colored Light Signals*—With the exception of the pyrotechnic type, all colored light signals are obtained from light sources combined with suitable color filters. Glide path indicators, traffic control projectors, airport beacons and identification and navigation lights on the plane are examples. The colors used for such lights are selected so as to be of high purity and to differ widely from one another in dominant wavelength. The pyrotechnic signals, owing to the greater difficulties in production and standardization of the colors, may differ less in dominant wavelength and may be of lower purity. The various colored light signals when viewed from a distance approximate point sources whose effective intensity decreases with the square of the distance. Consequently, even though objectively they differ widely in dominant wavelength and are of high purity, when seen from great distances or through fog or smoke, they may be difficult to distinguish because of the low intensity and the small visual angle subtended. They are also much more difficult to distinguish in the daytime, against the bright background of the sky, than when seen

against the night sky or other dark background. The person with deficient color discrimination may have greater difficulty than the normal person in detecting dim red lights, and he is likely to confuse red and amber, and green and white lights. It should be remembered, however, that the white lights are almost invariably of higher intensity than the green lights and when both are present the difference in brightness may provide an auxiliary clue.

*2 Identification of the Colors of Various Reflecting Surfaces Used as Daytime Signals*—This group includes flags, panels colored "shapes" (balls, triangles, pyramids and cones), vehicles painted in certain colors for the purpose of identification and colored smokes. With the possible exception of the smoke signals, these colors are also of high purity and differ widely in dominant wavelength. Such signals may become difficult to detect, and the different colors may be difficult to distinguish from one another because of the decrease in the visual angle subtended when they are viewed from a great distance, or because of decrease in the intensity, owing to such factors as atmospheric conditions. The colored cones, balls, triangles and pyramids used as signals as a rule are of specific shape for each color, so that identification may be possible even when the color is not distinguished.

*3 Identification of the Colors Used for Coding of Equipment*—Color coding is used, for example, to aid in the identification of fuel lines, oxygen lines and other aircraft piping. The colors used are red, yellow, white, green, blue, brown and black, in various combinations. Similar colors are used on gas cylinders. Identifying colors are also used for electric wires and fuses. The various colors used for coding are selected so as to show well marked differences. Special circumstances, such as dirt which obscures the colors, poor illumination or a small visual angle, may, however, increase the difficulty of identification by means of color. In many cases, clues other than color may be utilized. It is often possible to make the necessary identification of aircraft piping by means of differences in diameter, for example. The contents of gas cylinders are labeled in large white letters. Electric wires may be distinguished in some cases by diameter, by the presence or absence of marker threads or by attached tabs bearing distinguishing numbers. A continuity tester is also frequently used in tracing wires.

*4 Map Reading*—Varying shades of tan and green are employed in navigation maps to indicate elevation. The elevations of greatest importance are, however, always indicated by figures printed in black.

*5 Color Differences in Terrain, Both Natural and Camouflaged*—Various types of terrain, such as ploughed fields, sand, smooth grass

fields and swampy land, show differences in hue, in saturation and in brightness. Imperfectly camouflaged objects may differ from their backgrounds in a similar manner. Hendley and Hecht<sup>4</sup> measured the colors of natural objects and terrains. The colors were matched by direct comparison with the standard color chips in the Munsell Book of Color. The average color of forests, viewed from a distance of 1 or 2 miles (1,500 or 3,000 meters), was found, for example, to be 8.7 green-yellow in hue, 3.0 in value (brightness) and 1.5 in chroma (saturation). The color of distant objects "seen from two or more miles" was reported by them as 2.2 purple-blue in hue, 6.2 in value and 1.0 in chroma. According to these investigators,

because of the loss of saturation of distant objects, even the normal observer relies on brightness contrast for the principal clues in distinguishing objects at large distances. In hazy weather, all color may be lost when an object is viewed from as little as  $\frac{1}{4}$  of a mile.

Hendley and Hecht's measurements were made from the ground. In similar observations from a plane at high altitudes little loss in chroma was noted.<sup>5</sup> The differences in the results of the latter study are probably to be attributed to the greater clarity of the intervening atmosphere when one is looking directly downward from a plane.

The special difficulties experienced by subjects with defective red-green color vision in identifying terrain have perhaps been over-emphasized. It is frequently stated that such a subject will be unable to distinguish the blue-green color of swampy terrain from the yellow-green of a grass field. A moment's thought will show, however, that this particular situation involves discrimination of yellow and blue, not red and green. It should be emphasized that, even though differences in hue and saturation in different types of terrain may be slight, differences in "texture" or brightness are usually well marked. Relatively smooth surfaces, for example, reflect much more light than areas with thicker growth. In the technic of camouflage, the great emphasis on accurate control of "texture," shape and shadows, and the fact that photographs in black and white frequently provide as much information as does direct visual observation are further indications of the greater importance of differences in brightness than in those of chromaticity (hue and saturation).

In order to obtain further evidence on this point, a member of the Central Instructors School at Randolph Field, Texas, was asked

<sup>4</sup> Hendley, C. D., and Hecht, S. The Colors of Natural Objects and Terrains and Their Relation to Visual Color Deficiency, Office of Scientific Research and Development, Report no. 269, February 1944.

<sup>5</sup> History, Organization and Research Activities, Section V A, Color Vision, Staff Psychological Test Film Unit, Psychol. Bull. 41.457-468 (July) 1944 (p. 464).



to make a flight wearing red "dark adapter" goggles and to report any difficulties in judging the nature of the terrain. Although wearing of such goggles does not simulate deficiency in red-green color discrimination, it does effectively remove all differences in hue and may also distort the brightness differences slightly. The pilot, nevertheless, experienced no difficulty in identifying ploughed fields, various types of grass fields, etc., or in selecting suitable terrain for a forced landing. While this simple experiment was not extensive enough to be conclusive, it again indicates that in the case of natural terrain brightness differences alone may provide entirely adequate information as to its nature.

There have been occasional reports of persons with deficient color vision said to be actually superior to normal persons in the detection of camouflaged areas. In order to investigate this possibility, an experimental study was made by Wallace and associates<sup>6</sup> on the comparative efficiency of subjects with normal and subjects with deficient color vision in detecting panels painted with camouflage colors, when these were laid flat on the ground so as not to provide clues due to shadows, and the like. The results for the entire group revealed a definite relationship of number of errors to brightness difference between panel and background but no similar relation for differences in hue. The 10 subjects with deficient color vision, 3 of whom had dichromatic vision, were definitely, though only slightly, inferior to the subjects with normal color vision. The "average number of errors per run" for the normal group ranged from about 2.3 to 3 and that for the subjects with deficient color vision, from about 2.6 to 4.1. It is concluded in this report that the slight difference between the performance of subjects with normal color vision and that of subjects with deficient color vision may be of no practical significance, since under actual conditions the latter could make use of auxiliary clues, such as shadows, not present in the experimental situation.

In considering the types of color discrimination discussed here, it should be remembered that conditions differ in combat and in noncombat areas and vary with the type of duty involved. In drawing any conclusions as to the special handicap of the subject with defective red-green color vision in making these discriminations the possibility of auxiliary clues must be kept in mind. It should be remembered, also, that about three fourths of the group with deficient color vision have only partial defects for red and green discrimination, which

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6 Wallace, S. R., Hexler, P. L., and Hecht, S. Color Vision and Its Relation to the Detection of Camouflage, AAF Training Command Research Bulletin Hq 43-6, Oct 14, 1943

are of varying degrees of severity. For these reasons it cannot be dogmatically concluded that all persons with deficient color vision should be disqualified for any particular duty, such as that of a pilot or gunner. For the greatest efficiency in the selection of personnel, therefore, a quantitative test of color vision is needed which will classify persons with deficient color discrimination as to the degree of the defect.

An analysis of the type of color discriminations involved is of value in indicating what types of test may be expected to be most closely related to actual performance. It was found that the color discriminations fall into two more or less distinct categories. (a) There are those in which, objectively considered, the colors differ greatly in chromaticity but subjectively may be difficult to discriminate because of low intensity or small visual angle or both. Most of the colored light signals, the colored reflecting surfaces and the colors used in coding of equipment fall in this first group, (b) in the second category are the discriminations in which the colors involved are of low purity and differ only slightly in dominant wavelength but are in most cases of fairly high brightness and large area. The colors of the terrain are the best example of this type of discrimination. Colored smokes and map colors may also fall into this second category.

Ability to perform the color discriminations included in the first category may be expected to be most closely related to high scores in tests employing colors of high purity but of low intensity and small area. The discriminations in the second category, on the other hand, will probably be most closely simulated by tests which measure discrimination of hue or saturation for colors of low purity but of high intensity and large area. As will be seen in later sections of this paper, these facts were kept in mind in the selection of the battery of color vision tests investigated.

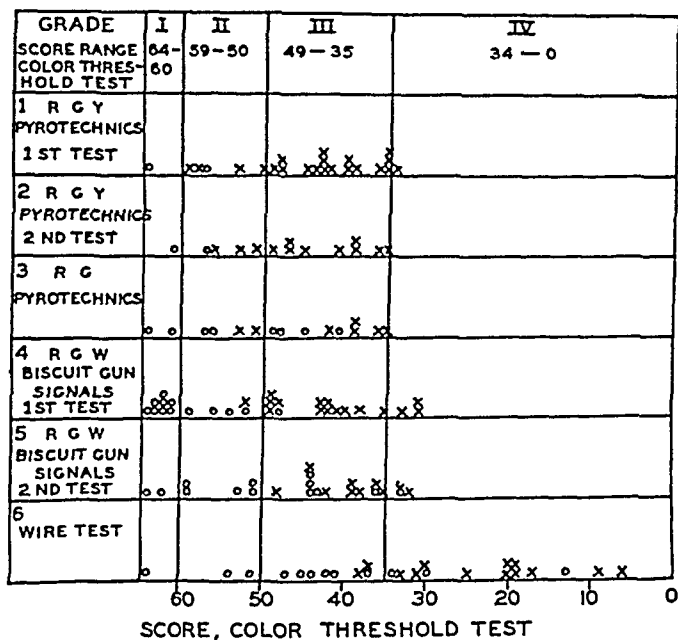
#### SELECTION OF TESTS FOR DETECTION OF AN ANOMALY IN RED-GREEN COLOR VISION AND FOR MEASUREMENT OF THE DEGREE OF THE DEFECT

A number of the available tests were investigated, and, where indicated, modifications were made in these tests. In addition, certain new tests have been developed for use in this study.

*American Optical Company Pseudo-Isochromatic Plates*—The series published by the American Optical Company consists of 46 plates, copied in some cases from the Ishihara series and in other cases from the Stilling series. The American Optical Company test, until December 1944 one of the official tests in use in the Army Air Forces, was found to be unsatisfactory in several respects. Some of the charts taken from

the Stilling series have digits whose form is somewhat unfamiliar to American readers. Other charts are unsatisfactory because of poor reproduction of the colors of the original plates.

In the early part of 1942 a study was initiated at the Army Air Forces School of Aviation Medicine to determine whether a simpler and more reliable test could be obtained by the elimination of a number of the charts. It was hoped that such a test might at least serve until something better could be developed. Preliminary studies indicated that errors in reading certain of the charts are not necessarily indicative of deficiency in color vision, since they are made about as frequently by those who read a majority of the charts correctly as by those who fail in a majority. On the other hand, other charts are unsatisfactory



Relationship between scores on Color Threshold Tester and ability to pass various practical tests

In this figure, *x* indicates failure to pass the practical test, *o* indicates that the subject passed the practical test. *R G Y* indicates red, green and yellow; *R G*, red and green; and *R G W*, red, green and white signals.

because they are frequently read correctly by those who fail in a majority of the charts.

Seventeen charts were selected which showed the highest consistency with the results obtained from the whole series. The abridged version recommended for adoption included 17 charts and 2 demonstration charts. In order to provide fewer clues for memorization, the charts were mounted on separate pages, so that they could be shown one at a time.

Similar studies were reported in the same year by Gallagher, Gallagher and Sloane.<sup>7</sup> The Royal Canadian Air Force<sup>8</sup> also proposed an abridged version of the American Optical Company test which consisted of 12 "essential" plates, used in diagnosing deficiency in color vision, combined with an additional 13 plates, which were not used in scoring. These were included in the series merely to make memorization more difficult. Selection of the 12 essential plates of the test used by Royal Canadian Air Force was based on its own data and those reported by the Army Air Forces School of Aviation Medicine and by Gallagher and associates. In 1944 the United States Navy issued for trial studies a new version of the American Optical Company charts. This series of 36 plates differs from the series recommended in the other investigations in that it is more than a mere selection of the better charts and incorporates several changes designed to increase the reliability of the test.

*Rabkin Polychromatic Plates*—This test, published in Russia, is similar in principle to the Ishihara, Stilling and other tests using pseudo-isochromatic charts. Geometric figures, such as circles, squares and triangles, are employed, as well as digits. The configuration of the digits conforms closely to American usage. One special chart (no 18) contains a number of green and brownish red squares, varying in brightness. Each horizontal row of squares contains either all green or all red squares. The brightness of the squares are so chosen that vertical rows of squares may be reported as of the same color by a person with defective color vision. Failure on this chart is probably indicative of a pronounced defect, since only a small per cent of the subjects with defective color vision make a definite selection of vertical rows when told to choose those containing squares of the same color. When the Rabkin test is used solely to differentiate subjects with normal from those with deficient color vision, considerable time is saved by the omission of this chart. In the present studies the two charts for detection of yellow-blue blindness were also omitted, since this type of defect is probably rare. The Rabkin test is difficult to obtain in this country at the present time. It was of particular value in this investigation as a check in doubtful cases, because there was no possibility that the subject could have been coached to pass this test.

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<sup>7</sup> Gallagher, J. R., Gallagher, C. D., and Sloane, A. E. A Critical Evaluation of Pseudo-Isochromatic Plates and Suggestions for Testing Color Vision, *Yale J. Biol. & Med.* **15** 79-98 (Oct.) 1942.

<sup>8</sup> Nicholls, J. V. V. RCAF Colour Plate Test, Report to Associate Committee on Aviation Medical Research, National Research Council of Canada, Ottawa.

*School of Aviation Medicine (S A M) Anomaloscope*<sup>9</sup>—This instrument is a modification of the Eastman Color Temperature Meter. One-half a circular field is illuminated by yellow light, the other half, by a mixture of red and green, the proportions of which can be varied. The instrument is of conveniently small size and can be purchased for about \$18. The substitution of another scale for the one graduated to read color temperature and the use of an auxiliary green filter to extend the range, although not absolutely essential, make the instrument more satisfactory for use as an anomaloscope. The test procedure used in these studies provides for three classifications: normal, moderately defective and markedly defective color vision. Subjects having a moderate defect may be further classified as deuteranomalous or protanomalous in type. Further details regarding the instrument, procedure and results are given in reports from the School of Aviation Medicine.<sup>9</sup>

*The Rand Anomaloscope (Bausch and Lomb)*—This instrument is still in the developmental stage. An experimental model was available for a short time during the course of color vision studies at the School of Aviation Medicine. If a test procedure is employed similar to that used in the S A M anomaloscope, two degrees of defect can also be distinguished by this test. A somewhat more elaborate test procedure can also be used, which may possibly provide finer classifications as to degree of defect.

*Inter-Society Color Council (ISCC) Single Judgment Test*<sup>10</sup>—In this test the observer is presented with a pair of chips and is required to say which chip of the pair is redder. The series contains 10 pairs of red chips which differ in saturation by small steps and 10 pairs of purple-red chips. In the form in which the test was used at the School of Aviation Medicine, the 10 pairs composed of red chips are shown first, then the 10 pairs composed of purple-red chips. The whole series is then presented a second time with the position of the pairs reversed from right to left. The complete test, therefore, requires a total of

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9 Rowland, L. S. A Simple Anomaloscope for Detecting and Classifying Red-Green Color Deficiencies, AAF School of Aviation Medicine, Project no 137, Report no 2, Randolph Field, Texas, July 29, 1943, Further Studies with a Simple Anomaloscope for Detecting Red-Green Color Deficiencies, AAF School of Aviation Medicine, Project no 137, Report no 3, Randolph Field, Texas, Sept 23, 1943. Dimmick, F. L. A Portable Anomaloscope for Screening Color Deficiency, J Optic Soc America **34** 352 (June) 1944. Sloan, L. L. The Eastman Color Temperature Meter Used as an Anomaloscope, *ibid* **34** 618-620 (Oct) 1944.

10 Hardy, L. Single Judgment Test for Red-Green Discrimination, J Optic Soc America **33** 512-514 (Sept) 1943.

40 judgments Preliminary studies with this test<sup>11</sup> indicated that the scores were not sufficiently reproducible to warrant its use as a means of measuring degrees of color deficiency It was further observed that some subjects with definitely deficient color vision were able to make perfect scores, probably because they made use of brightness rather than saturation differences and selected the darker chip as the redder Studies made by various members of the ISCC committee indicated that the second difficulty might be obviated if they returned to the procedure previously used and presented the red and purple-red chips alternately in random order No studies were made at the Army Air Forces School of Aviation Medicine using this procedure

*Eastman Hue Discrimination Test*—The essential principles of the test as used at the Army Air Forces School of Aviation Medicine may be described briefly The test target consists of a yellow Landolt C on a green background The target is superimposed on an evenly illuminated yellow-green "masking field" The test field seen by the subject, therefore, consists of a letter C composed of a mixture of yellow and yellow-green light, on a background composed of a mixture of green and yellow-green light When the brightness of the masking field is much greater than that of the target, the letter and background will be yellow-greens differing only slightly in hue The difference in hue is varied in fixed steps by variation in brightness of the masking field The test consists in determining the smallest difference in hue at which the subject can report correctly the orientation of the letter C

Thirty subjects with normal and 31 subjects with deficient color vision were tested with this instrument at the Army Air Forces School of Aviation Medicine Some overlapping was found in the scores of the two groups The few normal subjects who had as poor hue discrimination as some subjects with deficient color vision showed decided improvement on retests The test requires high concentration of attention and maximum cooperation, and it is probable that normal subjects occasionally make poor scores owing to inattention Several subjects with pronounced defects in color vision according to other tests showed relatively slight deviations from normal in this test One of these men reported that he was able to detect the break in the C because it was lighter than the rest of the ring but could distinguish no difference in color Another reported that the break was darker than the rest of the ring In a test field of the type used in this instrument very small brightness differences are discriminable Because of the difficulty of equating the brightness of the C and the background

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11 Rowland, L S An Evaluation of the ISCC Test for Color Deficiency in the Selection of Air Force Personnel, AAF School of Aviation Medicine, Project no 54, Report no 1, Randolph Field, Texas, May 29, 1942

for all subjects with deficient color vision of both protanopic and deutanopic types, it was concluded that further investigation of this test was not advisable

*Farnsworth-Munsell 100-Hue Test*<sup>12</sup>—The material used in this test consists of 85 color disks selected from a series of 100 Munsell papers which are equal in brightness and saturation but which vary in hue by small steps and cover the entire possible range of hues, i e., reds, yellows, greens, blues and purples. The color disks are presented in four groups, containing about 20 colors each. The task of the subject is to arrange each group in a graded series, varying, for example, from red to yellow or from yellow to green.

The results are plotted on a special graph. If this graph indicates poor hue discrimination for blues varying from reddish blue to greenish blue and for yellows varying from greenish to reddish yellow then a deficiency in red-green color vision is indicated. The relatively rare cases of yellow-blue blindness are also revealed by this test. Subjects with this defect show poor hue discrimination for reds varying from bluish red to yellowish red and for greens varying from bluish to yellowish. Some subjects have poor hue discrimination which is not clearly localized in two regions of the hue circle. A majority of these show deficiency in red-green color vision on other tests. Considerable time is required to record score and chart the results of this test. For this reason and because the results are sometimes difficult to classify as to type and degree of defect, the test was not used routinely in this investigation but was given only to certain subjects showing atypical responses on other tests.

*Terrain Test*<sup>13</sup>—The material of Farnsworth's test was used in devising the terrain test. This was designed to simulate the hue discriminations involved in identification of the colors of natural terrain. For this purpose, alternate chips in the series were selected ranging from red to yellow-red to green to bluish green. A total of 20 chips was used. As in the original test, the task of the subject was to arrange these in consecutive order. A simpler scoring system than that used by Farnsworth was adopted. If all the chips are arranged by the subject in the proper sequence, the score is zero with this method of scoring. Interchange of two chips gives an error score of 1, and in general the magnitude of the score increases with the degree of deviation from the correct order. The range of hues chosen for the terrain test was

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12 Farnsworth, D. The Farnsworth-Munsell 100-Hue and Dichotomous Tests for Color Vision, *J Optic Soc America* **33** 568-578 (Oct) 1943

13 Rowland, L. S. Selection and Validation of Tests for Color Vision. A Test for Ability to Distinguish Terrain Colors, AAF School of Aviation Medicine, Project no 137, Report no 1, Randolph Field, Texas, May 31, 1943

selected because it includes one of the two regions in which hue discrimination is poor for person with red-green color deficiency, and because the reds, yellows, greens and blue-greens used are representative of the colors of natural terrain. Further details with regard to the terrain test are given in the School of Aviation Medicine Report no. 1, project no. 137, May 31, 1943.

*Peckham Color Vision Test*—This is a color-matching test using 20 Munsell colors which appear equal in brightness and saturation to the normal person (value 5, chroma 4). The colors represent equal hue intervals on the Munsell color scale. A mechanical system permits the 20 hues to be compared in random order with each of the five standard hues, red, yellow, green, blue and purple. The subject's task is to report which pairs appear to him a perfect match. The normal subject should report as matched the 5 pairs which are identical and may include also those pairs which differ by one step in hue. Red and red yellow-red or green and green yellow-green, for example, might be reported a perfect match by a subject with normal color vision. A few normal subjects fail to report the supposedly identical colors as matched, presumably because of slight differences in the illumination falling on the two samples. Those with a pronounced deficiency in color vision may report as perfect matches colors which differ widely in hue, for example red and green or red and blue-green. Many subjects with deficient color vision give responses which cannot be differentiated from normal. It is probable that even when the subject with deficient color vision fails to see a difference in hue, the colors may appear to him slightly different in saturation or in brightness. It is easy to simulate normal color vision in this test if the subject with deficient color discrimination knows that only a few pairs of colors should match. Because of these and other objections to the test, it was not included in the battery of tests retained for further study.

*Tests of the Lantern Type*—Williams Lantern. A study of this instrument was made by Farnsworth and Reed<sup>14</sup>. They reported that the scores are difficult to interpret and correlate poorly with those for other tests and that the test does not distinguish observers with normal from those with moderately deficient color vision. Because of this unfavorable report, no study was made of this test at the School of Aviation Medicine.

*Canadian Lanterns*. The Royal Canadian Navy lantern employs red, green and white (actually yellow) test lights, subtending very small visual angles. Two test lights are shown at a time, and all

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<sup>14</sup> Farnsworth, D., and Reed, J. D. Examination of the Williams Lantern as a Test for Color Vision, Medical Research Laboratory, New London, Conn., Color Vision Report no. 6, Nov. 22, 1943.



9 possible pairs are shown. The test lights are approximately equal in intensity, with the exception of one less intense white of the pair of white lights. Farnsworth and Reed<sup>15</sup> reported that the test is simple to administer and to score. According to them, its only disadvantages are that (1) it does not distinguish types or degrees of color deficiency, (2) it allows some subjects with slight defects to pass as normal, (3) it does not detect malingerers effectively and (4) it requires a dark room.

The Royal Canadian Air Force recommended a modification of this lantern in which amber test lights were used in addition to red, green and white. The "Canadian Lantern test" studied at the School of Aviation Medicine is essentially similar to the test proposed by the Royal Canadian Air Force<sup>16</sup>. The procedure and method of scoring adopted after preliminary experiments were those found to give the highest reproducibility of scores and the best differentiation of subjects with normal and deficient color vision.

**Color Threshold Lantern<sup>17</sup>** This instrument was developed at the School of Aviation Medicine and differs from the Canadian and other lantern tests in several important respects. Each of the 8 test colors used is shown at 8 different intensities, the highest of which is approximately one hundred times the lowest. The minimum intensity differs for each color and is so chosen that a majority of subjects with normal color vision give the correct response at this level. At the lowest level of intensity the 8 test colors are therefore of approximately equal difficulty so far as recognition of the color is concerned. At the second level the intensities are double the minimum values, and at each succeeding level they are double those of the preceding one. The 8 colors are chosen so as to be representative of the permissible ranges for aviation colors. The 2 green test lights, for example, approximate the blue and yellow limits for aviation green. The method of scoring the test was selected so as to emphasize the difference in the responses of subjects with normal and with deficient color vision and so as to put a greater penalty on errors at high than at low levels of intensity.

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15 Farnsworth, D., and Reed, J. D. Trial of Royal Canadian Navy Colour Lantern in Comparison with Other Tests of Color Vision, Medical Research Division, New London, Conn., Jan 18, 1943.

16 Rowland, L. S. Selection and Validation of Tests for Color Vision. A Comparison of Two Lantern Tests for Red-Green Deficiency, the Color Threshold Lantern and a Modification of the RCN (Royal Canadian Navy) Lantern, AAF School of Aviation Medicine, Project no 137, Report no 4, Randolph Field, Texas, Oct 21, 1943.

17 Rowland, L. S. Selection and Validation of Tests for Color Vision. The Color Threshold Lantern as a Quantitative Test for Red-Green Color Deficiency, AAF School of Aviation Medicine, Project no 137, Report no 5, Randolph Field, Texas, Oct 20, 1943. Sloan, L. L. A Quantitative Test for Measuring Degree of Red-Green Color Deficiency, *Am J Ophth* **27** 941-947 (Sept) 1944.

## RESULTS OF INVESTIGATION

*Screening Tests*—Of the various tests investigated, those of the anomaloscope type and those employing pseudoisochromatic charts appear to be particularly suitable for use as screening tests because they are simple and can be given rapidly and because the percentage of failure on such tests is higher than that on other types of test which were studied

A study was made at the School of Aviation Medicine<sup>18</sup> in which the abridged American Optical Company test, the Rabkin test, and the S A M anomaloscope test were compared as to their efficiency as dichotomous tests for distinguishing normal from deficient color percep-

TABLE 1—Results of Three Screening Tests of Color Vision

| Rabkin Test, Number Errors | Anomaloscope and Abridged A O C* Tests |        | Abridged A O C Test, Number Errors | Anomaloscope and Rabkin Tests |        | Anomaloscope Point of Reversal | Rabkin and Abridged A O C Tests |        |
|----------------------------|--|--------|------------------------------------|-------------------------------|--------|--------------------------------|---------------------------------|--------|
|                            | Passed                                 | Failed |                                    | Passed                        | Failed |                                | Passed                          | Failed |
| 0                          | 63                                     | 0      | 0                                  | 64                            | 0      | 0                              | 49                              | 5†     |
| 1                          | 23                                     | 1†     | 1                                  | 25                            | 0      | $\pm 0.5$                      | 34                              | 4†     |
| 2                          | 1                                      | 0      | 2                                  | 6                             | 0      | $\pm 1.0$                      | 14                              | 1†     |
|                            |  |        | 3                                  | 2                             | 4†     |                                |                                 |        |
| 3                          |  | 1      |                                    |                               |        | $\pm 1.5$                      | 0                               | 4      |
| 4                          |  | 1      | 4                                  | 2†                            | 5      | $\pm 2.0$                      | 0                               | 9      |
| 5                          |  | 6      | 5                                  | 1†                            | 5      | $\pm 2.5$                      | 1†                              | 115    |
| 6                          |  | 6      | 6                                  |                               | 4      | $\pm 3.0$                      |                                 | 93     |
| 7                          |  | 6      | 7                                  |                               | 10     | $\pm 3.5$                      |                                 | 47     |
| 8                          |  | 15     | 8                                  |                               | 11     | $\pm 4.0$                      |                                 | 9      |
| 9                          |  | 17     | 9                                  |                               | 10     | $\pm 4.5$                      |                                 | 1      |
| 10                         |  | 32     | 10                                 |                               | 16     | No point of reversal           |                                 | 101    |
| 11                         |  | 53     | 11                                 |                               | 18     |                                |                                 |        |
| 12                         |  | 136    | 12                                 |                               | 17     | Total                          | 95                              | 389    |
| 13                         |  | 101    | 13                                 |                               | 21     |                                |                                 |        |
| Total                      | 97                                     | 380    | 14                                 |                               | 42     |                                |                                 |        |
|                            |  |        | 15                                 |                               | 43     |                                |                                 |        |
|                            |  |        | 16                                 |                               | 72     |                                |                                 |        |
|                            |  |        | 17                                 |                               | 100    |                                |                                 |        |
|                            |  |        | Total                              | 100                           | 383    |                                |                                 |        |

\* A O C indicates American Optical Company

† Nineteen subjects, indicated by daggers, gave inconsistent results on the three tests

tion The three color vision tests were scored according to the following standards

1 Abridged American Optical Company test 0 to 3 errors, pass, 4 to 17 errors, failure

2 Rabkin test 0 to 2 errors, pass, 3 to 13 errors, failure

3 S A M anomaloscope test scores between  $\pm 1.0$  and  $-1.0$ , pass, outside these limits, failure With these criteria, there is a close agreement in the classifications with the three tests Of the 495 subjects tested, 379 failed all three tests, 97 passed all three tests, and 19 gave inconsistent results The results are given in further detail in table 1

<sup>18</sup> Rowland, L S An Abridged Edition of the American Optical Company Plates for Testing Color Perception Comparison with Other Screening Tests, AAF School of Aviation Medicine, Project no 68, Report no 3, Randolph Field, Texas, May 8, 1945

The occasional subject who does not show consistent evidence of deficient color vision on all three tests is of especial interest from a theoretic point of view. Such a subject should receive further study in order to provide information as to the causes of the discrepancy and to determine whether it is perhaps indicative of a slight deviation from normal. The available data on the 19 subjects of this type are given in table 2. The relatively high scores made by a majority of these subjects on the Color Threshold Test indicates that in at least one particular aspect of color discrimination they differed little from normal.

TABLE 2—Data on Nineteen Subjects Giving Inconsistent Results on Three Screening Tests of Color Vision

| Subject Number | Errors in Abridged A O C * Test | Errors in Rabkin Test | Anomalous scope Point of Reversal | Score O T T †  | Comment  |
|----------------|---------------------------------|-----------------------|-----------------------------------|----------------|--|
| 1              | 4                               | 0                     | -0.5                              | Not determined |  |
| 2              | 4                               | 0                     | 0.0                               | Not determined |  |
| 3              | 5                               | 2                     | -0.5                              | 62             |  |
| 4              | 3                               | 2                     | +2.5                              | 56             |  |
| 5              | 3                               | 8                     | +2.5                              | 50             | Subject probably memorized some A O C charts   |
| 6              | 3                               | 8                     | +2.5                              | 48             | Subject probably memorized some A O C charts   |
| 7              | 3                               | 4                     | +3.0                              | 62             |  |
| 8              | 3(?)                            | 7                     | +3.5                              | 57             | On 6 A O C charts of dual response type subject saw both numbers with equal clearness, no other errors |
| 9              | 8                               | 1                     | +3.5                              | 62             |  |
| 10             | 6                               | 8                     | 0.0                               | 63             |  |
| 11             | 7                               | 3                     | 0.0                               | 63             | Normal responses also on Rand anomaloscope, 5 errors in recheck on Rabkin test                         |
| 12             | 8                               | 8                     | 0.0                               | 63             | Normal responses also on Rand anomaloscope, Farnsworth 100-Hue test shows definite defect              |
| 13             | 9                               | 10                    | 0.0                               | 59             |  |
| 14             | 9                               | 7                     | +0.5                              | 61             |  |
| 15             | 11                              | 8                     | 0.0                               | 63             | Normal response also on Hecht anomaloscope   |
| 16             | 11                              | 8                     | +1.0                              | 57             | Woman whose son also has deficient color vision  |
| 17             | 14                              | 12                    | +0.5                              | 40             |  |
| 18             | 15                              | 11                    | -0.5                              | 50             |  |
| 19             | 16                              | 13                    | +0.5                              | 64             |  |

\* A O C Indicates American Optical Company

† O T T Indicates S A M Color Threshold Test

It may be concluded that any one of the three tests will serve as an efficient screening test, since, with rare exceptions, subjects who fail one also fail the other two tests and since the exceptional cases are found primarily among subjects who have only a slight deficiency in color vision. In selecting one of the three tests for adoption as a screening test, several considerations are of importance. At the present time the Rabkin test is not available in this country in sufficient quantity to supply all the Air Force installations which would require them. If this test became generally distributed, as has been the case with the standard Ishihara and the American Optical Company tests, it would be easy to coach subjects to give the correct answers, since the Rabkin charts are so constructed that there are many auxiliary clues for memorization. If knowledge of the charts composing the abridged

American Optical Company test becomes available to the general public, its reliability will also suffer. Methods for training subjects with deficient color vision which aid them in reading such charts have recently been advocated. Dvorine,<sup>19</sup> for example, has published two volumes of such charts, one for training and one for testing. He reported that training on the first set of charts enables many subjects to read the charts of the second set. It is conceivable that there is sufficient transfer of training with some subjects to enable them to read with greater facility not only the charts on the Dvorine series but also those in other pseudo-isochromatic tests. Even if this does occur, however, it does not indicate any real improvement in color discrimination, which will extend to situations in which the required color discriminations differ significantly from those involved in reading such charts.

The methods of training in use at the present time do not, however, appear to be successful enough to present any serious problem. A total of 22 men who had taken some form of training which involved study of the standard American Optical Company and the Ishihara charts have been examined at the School of Aviation Medicine. The number of errors made in reading the 17 plates of the abridged test were, respectively, 16, 15, 15, 14, 14, 14, 13, 13, 10, 9, 8, 8, 7, 6, 6, 6, 6, 5, 5, 4, 4, and 3. Although the previous training probably resulted in fewer errors, only 1 of the 22 men was able to make a passing score.

It seems less likely that applicants could easily be coached to give normal responses on the anomaloscope test. This test would be of value, therefore, as a supplementary test, to be given to applicants whose responses in the abridged American Optical Company test indicated a questionable or borderline defect. It could also be used from time to time in "spot checks" to make sure that the abridged American Optical Company test was being properly given and that knowledge of the charts had not been disseminated among the applicants.

*Quantitative Tests*—The efficiency of a quantitative test of color vision to be used in the selection of aircrew personnel depends primarily on the reproducibility of the scores and the relationship of those scores to performance in the color discriminations actually required of such personnel.

The three tests evaluated in the previous section as possible screening tests also provide quantitative scores which could be used as an index of the degree of defect if shown to meet aforementioned criteria. Three other tests were extensively investigated in this study, the terrain test, the Canadian Lantern test and the Color Threshold Test. These tests

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<sup>19</sup> Dvorine, I. A New Diagnostic Method of Testing and Training Color Perception, *Am J Optometry & Arch Am Acad Optometry* **21** 225-235 (June) 1944

are not suitable for screening purposes because they are time consuming and because they do not detect all subjects with deficient color vision. They could, however, be used in conjunction with a preliminary screening test to determine the degree of defect in subjects who fail the preliminary test.

**A Reproducibility** The two pseudoisochromatic chart tests show high reproducibility in the number of errors made in two independent tests. A study at the School of Aviation Medicine in which the results obtained with natural daylight illumination were compared with illumination from daylight fluorescent bulbs gave indirect evidence that the error score made by any subject is a relatively constant quantity.<sup>20</sup> No detailed studies of the reproducibility of the scores with the S A M anomaloscope have been made. The Color Threshold Test, the Canadian Lantern test and the terrain test are in a sense performance tests rather than direct measures of color perception, and scores on these tests are in part determined by chance factors. It might be expected therefore that the scores would show a greater variation in successive tests. Actually, however, all three tests show a sufficient degree of reproducibility to warrant further study of their validity.

Studies at the School of Aviation Medicine<sup>21</sup> gave data on the test-retest correlation of the scores on the Color Threshold Test and the Canadian Lantern test. The subjects tested in that investigation included very few with pronounced defect, the correlation coefficients are, consequently, reduced by this limitation in range. Later data were, however, obtained for the Color Threshold Test based on a more representative range of defects. These data gave a test-retest correlation of 0.88 ( $N = 94$ ) for two tests made on different days, the interval between tests varying from one week to as much as six months. The earlier studies, on subjects showing a more limited range of defects, gave a correlation coefficient of 0.80 for the Color Threshold Test and 0.62 for the Canadian Lantern test ( $N = 43$ ). This difference, though not statistically significant for 43 cases, at least suggests a higher reliability for the Color Threshold Test. Use of the Pearson product moment formula to determine the reliability of the terrain test is not possible because the scores do not give a normal distribution. Data on 32 subjects (table 3) indicate that a scoring system for this test could be devised which would give a reliable measure of several degrees of color vision deficiency.

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20 Rowland, L. S. Daylight Fluorescent Lamps as a Source of Illumination in Tests of Color Perception with Pseudo-Isochromatic Plates, AAF School of Aviation Medicine, Project no. 130, Report no. 1, Randolph Field, Texas, April 1, 1943.

21 Rowland (footnotes 16 and 17)

B Validity An investigation of the relationship between scores on a number of tests of color vision and ability to identify "biscuit gun" signals is reported in detail in School of Aviation Medicine Research Project no 137, Report no 7<sup>22</sup> The six tests studied were the abridged American Optical Company Psuedo-Isochromatic Plates, the Rabkin Polychromatic Plates, the S A M Anomaloscope, the terrain test, the modified Canadian Lantern test and the S A M Color Threshold Test Thirty-four subjects with normal and 84 subjects with deficient color vision took part in these experiments The results indicated that only the last two tests gave scores which showed any relation to ability to identify biscuit gun signals and that the Color Threshold Test was

TABLE 3—*Scores on the Terrain Test for Thirty-Two Subjects*

| Scores     |             | Scores     |             | Scores     |             |
|------------|-------------|------------|-------------|------------|-------------|
| First Test | Second Test | First Test | Second Test | First Test | Second Test |
| 1          | 0           | 2          | 1           | 7          | 10          |
| 1          | 0           | 3          | 0           | 12         | 5           |
| 1          | 0           | 3          | 0           | 24         | 20          |
| 1          | 0           | 3          | 0           | 27         | 35          |
| 1          | 1           | 3          | 0           | 31         | 56          |
| 1          | 1           | 3          | 2           | 32         | 25          |
| 1          | 1           | 3          | 7           | 32         | 30          |
| 1          | 1           | 4          | 3           | 46         | 27          |
| 1          | 4           | 4          | 5           | 61         | 75          |
| 1          | 4           | 5          | 1           | 62         | 67          |
| 2          | 1           | 6          | 7           |            |             |

the better of the two in differentiating between those who could and those who could not distinguish the biscuit gun signals correctly

In a second study, the relationship between scores on the Color Threshold Test and ability to recognize colored pyrotechnic signals was investigated<sup>23</sup> In a third study, not previously reported, the relationship between scores on the Color Threshold Test and ability to identify electric wires by means of the colors used in the coverings was investigated A cable composed of 15 wires of 8 different colors was employed in these tests One wire in the bundle was shown to the subject by separating it from the others for an instant The subject was then

<sup>22</sup> Rowland, L S Selection and Validation of Tests for Color Vision Relationship Between Degree of Color Deficiency and Ability to Identify Signals from a "Biscuit Gun," AAF School of Aviation Medicine, Project no 137, Report no 7, Randolph Field, Texas, Nov 3, 1943

<sup>23</sup> Rowland L S Selection and Validation of Tests for Color Vision The Recognition of Pyrotechnic Signals by Normal and Color Deficient Subjects, AAF School of Aviation Medicine, Project no 137, Report no 6, Randolph Field, Texas, Nov 1, 1945

required to select this same wire from the complete bundle. Typical errors made by the subjects with deficient color vision were confusion of brown and red, blue and green, brown and green, and green and orange.

The relationships between scores on the Color Threshold Test and performance in the several practical tests are summarized in the accompanying chart. In this chart each cross or circle represents a subject with deficient color vision. Those who failed the particular practical test are indicated by crosses, those who passed, by circles. The location of the cross or circle on the horizontal meridian corresponds to the subject's score on the Color Threshold Tester. Inspection of the chart shows that discrimination of red, green and yellow pyrotechnic signals is a difficult task for the person with deficient color vision. No one with a score below 57 passed this test. Although a relatively small group took part in the tests in which only red and green pyrotechnics were used, the results suggest that the task is much easier for the subject with deficient color vision when yellow pyrotechnics are omitted. Of the 9 subjects making scores of 44 or higher, 7 passed this test.

In the first experiment with biscuit gun signals, 12 of the 13 subjects with scores above 50 passed the test, as compared with only 1 of the 16 subjects with scores below 50. The second test with biscuit gun signals does not show such a well marked differentiation. All those with scores above 50 passed, but a number with low scores also passed. A critical score of 50 would, therefore, not qualify men unable to discriminate red, green and yellow biscuit gun signals but would disqualify some who are able to do so. Identification of colored electric wires proved to be much easier than the identification of colored light signals. All subjects with scores above 40 and some with scores between 30 and 40 passed this test.

While the selection of qualifying scores for various tasks must be somewhat arbitrary until more extensive investigations are made, tentative critical scores provide the basis for distinguishing four grades of color deficiency in those who fail the pseudoisochromatic charts: grade 1, scores 64 to 60, grade 2, scores 59 to 50, grade 3, scores 49 to 35, grade 4, scores of 34 or less. The validating tests show that subjects with grade 4 scores make errors in identifying electric wires by color. Subjects with scores classified in grade 3 as a rule have only a partial defect for red and green. They are able to distinguish the colors of electric wires but will make errors in distinguishing red, green and white biscuit gun signals. Subjects with grade 2 scores will be able to distinguish red and green pyrotechnics if only those two colors are used. Subjects with grade 1 scores can distinguish red, green and yellow pyrotechnics.

## INDICATIONS FOR FURTHER STUDY

In the previous sections it has been shown that in the selection and classification of air force personnel two types of color vision tests are needed. The basic screening test should provide a simple, rapid and reliable means of distinguishing normal from deficient color vision. The second test, to be given only to subjects who fail the basic test, should give a reliable and valid estimate of the degree of defect.

The abridged American Optical Company test appears at present to be the most suitable choice for the basic test. Consideration should, however, be given to the future development of some form of screening test in which there is no possibility that the applicant could memorize the correct answers. The S A M anomaloscope might be a satisfactory substitute, although it is perhaps not so simple as chart tests. Unlearnable pseudoisochromatic charts might be constructed for example by using Landolt rings, the orientation of which could be changed. This principle has been employed in the Schaff test, published in France. A uniform pattern for the background in all charts as used in the new Navy test might be sufficient to prevent memorization.

Of the various quantitative tests investigated, the Color Threshold Test appears to be the most satisfactory for the classification of flying personnel, since the scores give a fairly reliable indication of ability to identify colored light signals. Data on the scores of a large group of subjects with deficient color vision not previously selected as to degree of defect would be of value in interpreting these scores on a percentile basis. Studies are also needed to provide further information as to the degree of defect in color vision compatible with the various duties of air force personnel.

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# OPHTHALMIC PENICILLIN OINTMENTS

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**F**AVORABLE reports have been made on the treatment of certain surface infections of the border of the lid, the conjunctiva and the cornea with penicillin ointments. Florey and Florey<sup>1</sup> used a penicillin salve with a pure petrolatum base. Keyes<sup>2</sup> applied penicillin in a wool fat and cold cream base, and Cashell<sup>3</sup> in a lanette wax base.<sup>4</sup> In an earlier experimental investigation in this laboratory<sup>5</sup> the penetrability of three ointments, representing two types of emulsion systems (anhydrous wool fat containing 10 per cent liquid petrolatum and an oil-in-water emulsion) was studied, similar investigations were conducted by Bellows<sup>6</sup> with four bases and by Leopold and LaMotte<sup>7</sup> with a Carbowax (a polyethylene glycol) base. The cited experimental studies were, however, concerned mostly with the penetration from a few ointments, generally containing the sodium salt of penicillin. It was desirable, therefore, to extend the investigations and to compare the advantages of several ointment bases and penicillin compounds.

In the present study three properties of penicillin ointments were collated experimentally: first, their irritative action on the normal

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1 Florey, M E, and Florey, H W. General and Local Administration of Penicillin, *Lancet* **1** 387 (March 27) 1943

2 Keyes, J. Penicillin in Ophthalmology, *J A M A* **126** 610 (Nov 4) 1944

3 Cashell, G T W. Penicillin in Ocular Infections, *Brit M J* **1** 420 (March 25) 1944

4 For a description of the lanette wax base, see the composition of base 6 in the section on "Technic"

5 von Sallmann, L, and Meyer, K. Penetration of Penicillin into the Eye, *Arch Ophth* **31** 1 (Jan) 1944

6 Bellows, J G. Penicillin Therapy in Ocular Infections, *Am J Ophth* **27** 1206 (Nov) 1944

7 Leopold, I H, and LaMotte, W O, Jr. Penetration of Penicillin in Rabbit Eyes with Normal, Inflamed and Abraded Corneas, *Arch Ophth* **33** 43 (Jan) 1945

rabbit and human eye, second, the stability of penicillin in various bases at room and at refrigerator temperature, and, third, the penetration of penicillin from the ointment into the eye. This subdivision is applied to the description of the experimental technic, as well as to the arrangement of the results. The problem of individual hypersensitivity to the mold product or to the ointment base was not dealt with, as it is of clinical nature, for the same reason, the first section on irritation was treated without reference to pathologic conditions of the eye.

#### TECHNIC

The investigations were limited to the sodium, calcium and ammonium salts of penicillin and to its free acid. With the exception of three salves supplied by pharmaceutical companies, the ointments were carefully made up in the pharmacy of the Presbyterian Hospital with a diversity of bases. When the sodium salt was used, it was dissolved in an appropriate dilution of the untag given on the vial. The activity of the calcium and ammonium<sup>8</sup> salts was titrated by bioassay and expressed in Oxford units per milligram of the material. Weighed quantities were dissolved in calculated amounts of sterile isotonic solution of sodium chloride or were suspended in liquid petrolatum U S P to obtain ointments of the hydrous (1 per cent moisture) or the anhydrous type, containing 1,000 Oxford units of penicillin per gram. Five of the salves were prepared with a hydrous and four with an anhydrous base. After the incorporation of the aqueous solution or oily suspension into the base and thorough mixing of the ingredients, the ointments were dispensed in collapsible tubes. One set was stored in the refrigerator at 32 F and the other at a room temperature of 70 to 85 F. The preparations were tested within a week after they had been made, and the tests were repeated at intervals of four to sixteen weeks.

The sodium, ammonium and calcium salts of penicillin were incorporated in four to six, and the free acid in one, of the following bases:

1 Wool fat-petrolatum base, hydrous

|                         |    |
|-------------------------|----|
| Liquid petrolatum U S P | Gm |
| Wool fat U S P          | 10 |
| White petrolatum        | 50 |
|                         | 40 |

2 Wool fat-petrolatum base, anhydrous

3 S base, anhydrous

|  |    |
|--|----|
| Light liquid petrolatum U S P (Kaydol) | Gm |
| Wool fat U S P                         | 14 |
| Petrolatum (grade Protopet no 1)       | 10 |
|  | 36 |

4 Wool fat-cold cream base

|                |    |
|----------------|----|
| Wool fat U S P | Gm |
| Cold cream     | 25 |
|                | 75 |

Cold Cream

|                              |       |
|------------------------------|-------|
| Spermaceti (cetyl palmitate) | 6 Gm  |
| White wax                    | 12 Gm |
| Liquid petrolatum            | 50 Gm |
| Sodium borate                | 1 Gm  |
| Distilled water              | 20 cc |

5 Hydrosorb—oleic acid ester, amide of diethanolamine, oleic acid and white petrolatum

6 Lanette wax base

<sup>8</sup> Dr Karl Meyer, of the department of ophthalmology, Columbia University College of Physicians and Surgeons, suggested the use of the ammonium salt of penicillin.

|                         |    |
|-------------------------|----|
| N octadecyl alcohol     | Gm |
| Sodium lauryl sulfonate | 45 |
| Cetyl alcohol           | 10 |
| White petrolatum        | 45 |
| Liquid petrolatum       | 50 |
| Water                   | 75 |
|                         | 75 |

7 Vegetable oil base, hydrous This base consists of hydrogenated peanut, soy bean and cottonseed oils

8 Vegetable oil base, anhydrous

9 L base, anhydrous This base consists of Amerchol and petrolatum Amerchol represents the nonsaponifiable residue of wool fat and is a mixture of sterols and sterol esters

The irritative action on the conjunctival sac of normal rabbits after application of the ointments for two hours was judged by the presence and amount of hyperemia and secretion of the conjunctiva and occasionally by a slight haziness of the cornea. From parallel observations on the action of ointments containing the same salt but in different bases, it was possible to determine which component was responsible for the irritation. The tolerance of the human eye to the respective salves was determined by the same criteria and by the presence of symptoms of discomfort in 5 volunteers.

The stability of the penicillin in the ointment was evaluated after extraction from accurately weighed amounts of the ointment.<sup>9</sup> The samples were transferred to a separatory funnel, which contained 50 cc of chloroform and 25 cc of phosphate buffer (0.15 molar primary and 0.15 molar secondary phosphate in a proportion of 6:4). After the mixture had been shaken for five minutes and the fluids had settled, the chloroform was drained off and washed again with 25 cc of the buffer solution. The extracts were combined in a centrifuge bottle, and remnants of the chloroform were thrown down by centrifugation for five minutes. In all steps of the procedure care was taken to keep the temperature low, the samples were placed on ice, the centrifuge bottles remained in the refrigerator and in one series they were spun in a low temperature centrifuge. Proportions of ointment and buffer solution were calculated to render a dilution of the incorporated penicillin to 10 Oxford units per cubic centimeter. Further dilutions of this solution were made, and the average of triplicate readings, obtained with the Oxford cup method, was computed against the standard curve for the day. It was calculated that approximately 15 per cent of the penicillin activity was lost during the procedure of extraction, but, since the initial penicillin content was taken as the amount of penicillin determined after the first extraction and therefore included this loss, as did subsequent determinations, it was not necessary to subtract it from each figure.

The penetration of penicillin from the ointments into the eye was studied on rabbits. For this purpose, the ointments were placed in the conjunctival sac, and aqueous fluid was withdrawn two hours later to estimate its antibacterial activity. For standardizing the technic, the following experimental conditions were observed. Light ether anesthesia was administered and was supported by the instillation and subcutaneous injection of 0.1 per cent nupercaine hydrochloride at the lid border prior to the insertion of two mattress sutures at corresponding positions in the margins of the upper and lower lids. While the lids were retracted, the ointment was squeezed from the tube and placed at the limbus in a way that a ribbon of the ointment circled twice the circumference of the cornea. Then the lids were closed by tying the sutures. After two hours the sutures and excess ointment were removed. Local anesthesia was again induced with nupercaine for withdrawal of aqueous, or the rabbits were killed for the

<sup>9</sup> Dr Karl Meyer furnished the technic of extraction and made other helpful suggestions.

excision of the cornea and conjunctiva. Usually 0.2 cc of undiluted aqueous was used to ascertain the penicillin content with the Oxford cup method in four to six experiments for each ointment. In one series, in which the cornea and conjunctiva were tested for the presence of penicillin, extracts of these tissues were obtained in buffer solutions by grinding them with quartz sand.<sup>5</sup>

## RESULTS

*Irritation*—In general, the ointment bases and penicillin compounds which were examined were well tolerated by the normal rabbit and human eye. A transient stinging and burning sensation which was noted occasionally was considered negligible. It was more intense, however, with salves made with the Hydrosorb base. With this base, hyperemia, and in some instances a moderate degree of chemosis and a fine haze, of the cornea were noticed. The ammonium salt made up in the hydrous vegetable oil base (7) caused slight soreness, lasting for several hours, whereas the same salt in other bases was not irritating. None of the ointments gave rise to a conspicuous lesion of the corneal epithelium, such as Bellows described after the application of a vanishing cream. The rancid smell of the ointment containing the calcium salt in the anhydrous vegetable oil base (8) would make the preparation unsuitable for practical use.

*Stability*—To our knowledge, there are no reports in which the decrease in activity of penicillin in ophthalmic ointments was determined with quantitative methods. The occasionally applied examination of the potency of the preparation by placing samples on seeded plates and observing the zones of inhibition is too crude to permit reliable conclusions. The decline in the activity of penicillin after various intervals of time is presented in table 1. The inactivation is expressed in per cent of loss from the initial penicillin activity as determined in the first week after the compounding of the ointment. The importance of the temperature of storage is evident in all instances except that of the ointment containing the calcium salt in the L base (9). In this ointment the salve retained 71 per cent of its initial activity after storage for twelve weeks at room temperature, another base containing the ammonium salt in the S base (3) retained 24 per cent of its initial activity at the same interval. The gradient of decline varied in the other preparations, but in most samples only traces<sup>10</sup> of penicillin activity were evident at the four or eight week interval.

When the ointments were stored in the refrigerator, the decrease in activity was much less but varied considerably with the salt and the base. With the sodium salt a minimal loss in the potency of the ointment was estimated for the hydrous vegetable oil base (7). Only 26 per cent of its initial penicillin activity was lost after storage for sixteen weeks, whereas with the anhydrous vegetable oil base (8), the

<sup>10</sup> The term "trace" is applied here to the inhibition of growth within the cup in the Oxford method of penicillin determination.

hydrous wool fat-petrolatum base (1) and the wool fat-cold cream base (4)<sup>11</sup> the losses ranged between 40 and 50 per cent after twelve weeks' storage. The ointments containing the ammonium salts also retained their activity well when prepared in the hydrous vegetable oil base (7). After twelve weeks no inactivation was noticed. The S base (3) and the anhydrous vegetable oil base (8) were less stable, with a loss of 31 to 44 per cent in their penicillin activity at the end of the same period.

The ointments with the calcium salt showed an optimum of stability as manufactured in the L base (9). In this preparation no appreciable

TABLE 1—*Loss of Penicillin Activity in Ointments at Refrigerator and Room Temperatures*

| Penicillin Compound | Ointment Base                  | Type of Storage  | Per Cent Loss of Initial Penicillin Activity After |         |         |       |
|---------------------|--------------------------------|------------------|--|---------|---------|-------|
|                     |                                |                  | 4 Wk   | 8 Wk    | 12 Wk   | 16 Wk |
| Sodium Salt         | Wool fat-petrolatum, hydrous   | Refrigerator     |  | 36      | 43      | 49    |
|                     |                                | Room temperature |  | 49      | 72      | T     |
|                     | Wool fat-petrolatum, anhydrous | Refrigerator     |  | 71.9    | T       |       |
|                     |                                | Room temperature |  | T       |         |       |
|                     | Wool fat-cold cream            | Refrigerator     | 20   | 24      | 44      |       |
|                     |                                | Room temperature | 63   |         | T       |       |
|                     | Vegetable oil base, hydrous    | Refrigerator     | No loss  | 7       | 10      | 26    |
|                     |                                | Room temperature | 14   | T       |         |       |
| Ammonium Salt       | Vegetable oil base, hydrous    | Refrigerator     |  | 18      | 43      |       |
|                     |                                | Room temperature |  | T       |         |       |
|                     | Vegetable oil base, anhydrous  | Refrigerator     | No loss  | No loss | No loss | 32    |
|                     |                                | Room temperature | T  |         |         |       |
|                     | S base                         | Refrigerator     |  | 15      | 31      |       |
|                     |                                | Room temperature | T  |         |         |       |
|                     | L base                         | Refrigerator     | 5  | 18      | 44      |       |
|                     |                                | Room temperature | 12   | 40      | 76      |       |
| Calcium Salt        | Vegetable oil base, hydrous    | Refrigerator     | 56   |         | 67      |       |
|                     |                                | Room temperature | T  |         |         |       |
|                     | Vegetable oil base, anhydrous  | Refrigerator     | 8  |         | 30      |       |
|                     |                                | Room temperature | T  |         |         |       |
|                     | S base                         | Refrigerator     | 18   |         | 43      |       |
|                     |                                | Room temperature | T  |         |         |       |
|                     | L base                         | Refrigerator     |  | No loss | No loss |       |
|                     |                                | Room temperature |  | No loss | 29      |       |
| Free Acid           | S base                         | Refrigerator     | 4  | 9       | 15      |       |
|                     |                                | Room temperature | 35   | 53      | T       |       |

T = reduced to a trace of penicillin activity

decrease in activity was noticed at refrigerator temperature twelve weeks after the first determination. The hydrous vegetable oil base (7) lost 67 per cent, the anhydrous vegetable oil base (8) lost 30 per cent and the S base (3) lost 43 per cent, of the initial penicillin potency at the same interval.

The free acid was supplied only in one base (3). At refrigerator temperature the decrease in activity was moderate, that is, it lost 15 per cent after twelve weeks.

11 Tentative experiments revealed that spermaceti, a constituent of the wool fat-cold cream base, inhibited the activity of penicillin. A 1 per cent solution of this ingredient caused a 50 per cent loss in the potency of a penicillin solution containing 10 Oxford units per cubic centimeter.

Experiments with ointments containing the sodium salt in a lanette wax base (6) were discontinued because the separation of the aqueous phase in the emulsion system resulted in great variations in the penicillin content of gravimetrically indential samples of the ointment

In conclusion the experiments on the stability of four penicillin compounds in various ointment bases showed the superiority of two types of ointments the hydrous vegetable base with the sodium and ammonium salts and the L base, which was supplied with the calcium salt The latter was the only preparation which retained much of its original potency after storage for twelve weeks at room temperature These investigations on the stability of ophthalmic ointments disclosed no specific advantage in the use of any particular salt of penicillin or its free acid

Determinations were not continued over a longer period of storage because, with the intensive investigations of the many commercial research laboratories in the manufacture of ophthalmic penicillin ointments, it is likely that such a product which is stable at unfavorable temperatures will be available in the near future In view of this, greater emphasis was placed on the experiments relating to the resorption of penicillin from the various ointment bases into the eye

*Penetration*—The penetration of penicillin into the cornea and the conjunctiva was investigated in a series of 12 eyes It was technically impossible to remove completely the excess ointment from the surface of the tissues without changing the content of penicillin in the specimens This and other inaccuracies in handling and extracting the ground tissue led to such erratic results that further measurements were not attempted Readings on the antibacterial activity of the aspirated aqueous were more consistent and are shown in table 2

When ointments with the sodium salt of penicillin were used, the highest average concentration of penicillin in the aqueous (0.6 Oxford unit per cubic centimeter) was determined by the resorption from the lanette wax base (6), but the values were very low in 2 instances The discrepancy in the results can be explained by the instability of the ointment base, as described in the previous section The penetration from the hydrous vegetable oil base (7) was satisfactory, with an average of 0.51 Oxford unit per cubic centimeter of aqueous Resorption from the wool fat-cold cream base (4) was about one-half that from the hydrous vegetable oil base Only traces of penicillin activity were estimated, however, with the wool fat-petrolatum bases (1 and 2) and with the vegetable oil base prepared with an anhydrous base (8)

In contrast to the poor penetration of sodium penicillin in the anhydrous wool fat-petrolatum base (2) was that of the ammonium salt in a similar base (3) Here relatively high readings were recorded with 0.61 Oxford unit per cubic centimeter of aqueous The

concentration of 0.53 Oxford unit, determined after the use of the ammonium salt in the hydrous vegetable oil base (7), was similar to that after the application of the sodium salt in the same base. The

TABLE 2—*Penetration of Penicillin into the Aqueous Two Hours After Placing Ointment in Conjunctival Sac*

| Penicillin Compound | Ointment Base                 | Oxford Units Penicillin per cc Aqueous |
|---------------------|-------------------------------|--|
| Sodium Salt         | Wool fat-petrolatum, hydrous  | Traces *                               |
|                     | Wool fat-petrolatum, hydrous  | Traces                                 |
|                     | Wool fat-cold cream           | 0.18                                   |
|                     |                               | 0.46                                   |
|                     |                               | 0.23                                   |
|                     |                               | Trace                                  |
|                     | Average                       | 0.23                                   |
|                     | Lanette wax                   | 0.24                                   |
|                     |                               | 0.69                                   |
|                     |                               | 1.43                                   |
|                     |                               | Trace                                  |
|                     | Average                       | 0.6                                    |
|                     | Vegetable oil base, hydrous   | 0.44                                   |
|                     |                               | 0.32                                   |
|                     |                               | 0.63                                   |
| Ammonium Salt       |                               | 0.63                                   |
|                     | Average                       | 0.51                                   |
|                     | Vegetable oil base, anhydrous | Traces                                 |
|                     | S base                        | 1.0                                    |
|                     |                               | 0.83                                   |
|                     |                               | 0.64                                   |
|                     |                               | 0.48                                   |
|                     |                               | 0.56                                   |
|                     |                               | 0.17                                   |
|                     | Average                       | 0.61                                   |
|                     | Vegetable oil base, hydrous   | 0.89                                   |
|                     |                               | 0.1                                    |
|                     |                               | 1.0                                    |
|                     |                               | 0.79                                   |
|                     |                               | 0.2                                    |
| Calcium Salt        |                               | 0.15                                   |
|                     | Average                       | 0.53                                   |
|                     | Vegetable oil base, anhydrous | 0.19                                   |
|                     |                               | 0.15                                   |
|                     |                               | 1.38                                   |
|                     |                               | Trace                                  |
|                     |                               | Trace                                  |
|                     |                               | Trace                                  |
|                     | Average                       | 0.29                                   |
|                     | S base                        | Traces                                 |
|                     | Vegetable oil base, hydrous   | 0.99                                   |
|                     |                               | 0.41                                   |
|                     |                               | 0.41                                   |
|                     |                               | 1.75                                   |
|                     | Average                       | 0.89                                   |
| Free Acid           | Vegetable oil base, anhydrous | 0.15                                   |
|                     |                               | Trace                                  |
|                     |                               | 0.27                                   |
|                     |                               | Trace                                  |
|                     | Average                       | 0.13                                   |
|                     | L base                        | 0.6                                    |
|                     |                               | 0.53                                   |
|                     |                               | 1.22                                   |
|                     |                               | 0.8                                    |
|                     | Average                       | 0.79                                   |
|                     | S base                        | Traces                                 |

\* Trace indicates 0.05 Oxford unit

penicillin content of the aqueous after the use of the ointment with the anhydrous vegetable oil base (8) was about one-half that obtained with the hydrous type of this base

The best penetration from ointments containing the calcium salt was ascertained with the hydrous vegetable oil base (0.89 Oxford unit per cubic centimeter of aqueous). Slightly lower (0.79 Oxford unit per cubic centimeter of aqueous) was that from the L base (9), whereas the resorption from the anhydrous vegetable oil base (8) and from the S base (3) was very little. Equally unsatisfactory was the resorption from the latter base containing the free acid (0.08 Oxford unit per cubic centimeter). In general, the penetration of penicillin into the eye was highest from ointments containing the calcium salt, less from ointments with the sodium and ammonium salts and lowest from the one ointment with the free acid.

Because of the differences in the technics it is scarcely possible to compare the results of this study with previous investigations on the penetration of penicillin from ointments into the eye. In earlier experiments reported by this laboratory the ointments which were used contained penicillin of very low potency and the aqueous did not exhibit any antibacterial activity. Leopold and LaMotte,<sup>7</sup> using an ointment containing 500 Oxford units of sodium penicillin per gram of Carbowax base (polyethylene glycol), also did not detect any inhibitory action of the aqueous in normal rabbit eyes. Bellows'<sup>6</sup> experiments disclosed a concentration of 0.42 Oxford unit of penicillin per cubic centimeter of aqueous with a wool fat ointment and 0.38 Oxford unit per cubic centimeter with an oil-in-water emulsion. Both ointments contained 2,500 Oxford units of sodium penicillin per gram of base and were not irritating.

The composition of the wool fat-petrolatum base (1) used in the present study was similar to that applied by Bellows but gave the lowest values for penicillin in the aqueous, as only traces could be determined. The penicillin content of this ointment declined to about one half of its original potency after sixteen weeks' storage in the refrigerator. Despite the lower unitage in our preparations, the penicillin concentration of the aqueous after the application of several ointments ranged slightly higher than that reported by Bellows. Significantly greater, however, were the figures obtained after the application of the stable salve containing the calcium salt in the L base (9).

In conclusion, of the many penicillin ointments tested, the requirements for a nonirritating, relatively stable and well penetrating preparation for ophthalmic use were best fulfilled by the following bases: the hydrous vegetable oil base (7), with the sodium salt, and the L base (9), supplied only with the calcium salt.



## SUMMARY

1 Of the series of nine ointment bases which were tested, two were irritating to the eye. No irritation could be attributed to any of the four penicillin compounds which were incorporated in the ophthalmic ointments.

2 The potency of the penicillin in the salves was relatively stable in one hydrous and two anhydrous bases after twelve to sixteen weeks in the refrigerator. Storage at room temperature resulted usually in a rapid loss of potency except for two ointments prepared with an anhydrous base. No difference in the stability of the various ointments could be ascribed to the penicillin compound in the salves.

3 The penetration of penicillin into the aqueous of rabbits was substantial from one hydrous and two anhydrous bases. After the application of two ointments with the calcium salt, the content of penicillin in the aqueous exceeded that after the use of salves with the sodium and ammonium salts. The resorption of penicillin was unsatisfactory from the one ointment which contained the free acid of penicillin.

The Schering Corporation supplied the ammonium salt of penicillin and the ointments containing the free acid and the ammonium salt in the S base, and the Lederle Laboratories, Inc., the ointment containing the calcium salt of penicillin in the L base.

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# EFFECTS OF ATROPINE SULFATE, METHYLATROPINE NITRATE (METROPINE) AND HOMATROPINE HYDROBROMIDE ON ADULT HUMAN EYES

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CERTAIN details of the clinical actions of several mydriatics of the belladonna group are given in tables in the textbooks of pharmacology of Sollmann<sup>1</sup> and Goodman and Gilman,<sup>2</sup> but the relative speeds and durations of the actions of the various drugs are not well defined because (a) the solutions used varied in strength from 0.5 to 10 per cent and (b) doses are not given. It appeared desirable, therefore, to gather data permitting a more exact comparison of the actions of some of these drugs. Atropine seemed the logical choice as the standard with which homatropine and methylatropine nitrate (Metropine) should be compared.

Of the many authors who have described the mydriatic and cycloplegic effects of atropine, homatropine and methylatropine nitrate, only a few have given data pertinent to the present investigations. Consideration of dosage being omitted for the moment, the time for maximal effect and the approximate time of recovery may be briefly described. Atropine produces maximal mydriasis in about thirty to forty minutes, with complete recovery in twelve days, and maximal cycloplegia in a few hours, with recovery in a few days to perhaps as long as eighteen days (Marron<sup>3</sup>). Homatropine produces maximal mydriasis in seven to thirty minutes, with recovery in six to ninety-six hours, and maximal cycloplegia in thirty to ninety minutes, with recovery in ten to forty-eight hours (Bertheau,<sup>4</sup> Jackson,<sup>5</sup> Marron,<sup>3</sup> Risley,<sup>6</sup> Schell<sup>7</sup> and Tweedy and Ringer<sup>8</sup>).

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1 Sollmann, T. A Manual of Pharmacology and Its Application in Therapeutics and Toxicology, Philadelphia, W. B. Saunders Company, 1942.

2 Goodman, L., and Gilman, A. Pharmacological Basis of Therapeutics, New York, The Macmillan Company, 1941.

3 Marron, J. Cycloplegia and Mydriasis by Use of Atropine, Scopolamine and Homatropine-Paredrine, Arch. Ophth. **23** 340 (Feb.) 1940.

(Footnotes continued on next page)

Methylatropine nitrate produces approximate maximal mydriasis in thirty to seventy-five minutes, with recovery in forty to seventy-two hours, and maximal cycloplegia in two to fourteen hours, with recovery in thirty-six hours (Goldberg,<sup>9</sup> Lindenmeyer<sup>10</sup>) These data illustrate the general opinion that atropine is much more lasting in its effects on the eye than is homatropine or methylatropine nitrate

We were interested in comparing the mydriatic and cycloplegic effects of these three drugs on human eyes that had received the same dose of each drug Goldberg<sup>9</sup> had compared equal strengths of homatropine and methylatropine nitrate against solutions of atropine only one-tenth as concentrated Blume<sup>11</sup> had used 1 per cent solutions of each of the three drugs in the eyes of cats Our technic was to instil a single drop of a solution of 1 per cent atropine sulfate, 1 per cent methylatropine nitrate or 1 per cent homatropine hydrobromide A series of 46 eyes were studied, the distribution according to the patients' ages being shown in the following tabulation

| Patient's Age, Yr | Number of Eyes |
|-------------------|----------------|
| 16-20             | 8              |
| 21-25             | 22             |
| 26-30             | 12             |
| 31-37             | 4              |

Diameters of the pupils were generally measured with a V pupilometer under fairly uniform lighting conditions With 6 eyes entoptic pupillometry (Cogan<sup>12</sup>) was employed With the two methods pupillary diameters were reproducible within 0.5 mm Amplitude of accommodation was measured by the difference of near and far point reciprocals Six point newsprint on a slide on a meter stick was used to ascertain these points When necessary, a lens sufficient to keep the far point between 0.66+ and 1 meter from the eyes was added to the system

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- 4 Bertheau, H    Das Homatropin, Berl klin Wchnschr **17** 581, 1880
  - 5 Jackson, E    Homatropin Hydrobromate, M News, Philadelphia **49** 88, 1886
  - 6 Risley, S D    The Value of Homatropine Hydrobromate in Ophthalmic Practice, Am J M Sc **81** 113, 1881
  - 7 Schell, H S    A New Mydriatic, Philadelphia M Times **11** 7, 1880
  - 8 Tweedy, J, and Ringer, S    Mydriatic Properties of Homatropin, or Oxytoluyltropin Its General Physiological Action, Lancet **1** 795, 1880
  - 9 Goldberg, H    Versuche mit Eumydrin, einem Ersatzmittel des Atropin-sulfates, Heilkunde **7** 97, 1903
  - 10 Lindenmeyer, O    Eumydrin, ein neues Mydriaticum, Berl klin Wchnschr **40** 1072, 1903
  - 11 Blume, W    Ueber eine die Pupille verengende Wirkung des Atropins, Arch f exper Path u Pharmacol **164** 226, 1932
  - 12 Cogan, D G    A Simplified Entoptic Pupillometer, Am J Ophth **24** 1431, 1941

The solutions were administered according to the plan shown here-with Each subject in the study received one drug in his right eye and the same or another drug in his left eye

| No of Pairs of Eyes | Right Eye                | Left Eye               |
|---------------------|--------------------------|------------------------|
| 11                  | Atropine sulfate         | Methylatropine nitrate |
| 2                   | Atropine sulfate         | Atropine sulfate       |
| 7                   | Homatropine hydrobromide | Methylatropine nitrate |
| 2                   | Methylatropine nitrate   | Methylatropine nitrate |
| 1                   | Control                  | Methylatropine nitrate |

The anisopia bothered some of the subjects considerably and made walking and grasping objects somewhat uncertain For example figure 1 illustrates the different amounts of mydriasis obtained in a subject who received atropine in his right eye and methylatropine in his left eye

Figures 2, 3 and 4 show the data for changes in time of accommodation and in size of pupils During the first hour represented by each curve, readings were made at short intervals (abscissas, in minutes),



Fig 1—Mydriasis produced in the right eye by 1 drop of 1 per cent solution of atropine sulfate and in the left eye by 1 drop of a 1 per cent solution of methylatropine nitrate

additional readings were made at six hours and thereafter up to fourteen days for atropine and methylatropine and up to eleven days for homatropine Although many eyes were followed for up to fourteen days, measurements were discontinued as the values for each subject approached the original normal values

To allow the curves for mydriasis and cycloplegia to run parallel courses, the units of accommodation plotted were  $100/D_t$ , where  $D_t$  was the number of diopters of accommodation at any time,  $t$  This allows somewhat more satisfactory inspection of the graphs Various subjects have characteristic marks in these figures, so that the course of the effects on one person may be followed through the entire period The general trends for each drug are similar, but variation in individual responses is clearly shown by the wide scatter of points above and below the trend lines which are indicated In figure 5 the average curves are reproduced so that the comparative effects of atropine, homatropine and methylatropine are shown side by side

*Average Mydriatic and Cycloplegic Effects of Atropine, Methylatropine Nitrate and Homatropine*

| Drug           | Number of Eyes | Initial Pupillary Diameter ( $P_0$ ) | Time to Maximum |             | Maximum Pupillary Diameter ( $P_t$ ) | Maximal Dilation Ratio ( $P_t/P_0$ ) | Time to Onset of Recovery of |             | Residual Accommodation ( $D_t/D_0$ ) | Fifth Day                    |                              |                                      |
|----------------|----------------|--------------------------------------|-----------------|-------------|--------------------------------------|--------------------------------------|------------------------------|-------------|--------------------------------------|------------------------------|------------------------------|--------------------------------------|
|                |                |                                      | Mydriasis       | Cycloplegia |                                      |                                      | Mydriasis                    | Cycloplegia |                                      | Pupillary Diameter ( $P_t$ ) | Dilation Ratio ( $P_t/P_0$ ) | Residual Accommodation ( $D_t/D_0$ ) |
|                |                |                                      |                 |             |                                      |                                      |                              |             |                                      |                              |                              |                                      |
| Atropine       | 16             | 3.4                                  | 10 min          | 5 hr        | 8.3                                  | 2.44                                 | 6 hr                         | 1 day       | 0.21                                 | 5.2                          | 1.51                         | 0.60                                 |
| Methylatropine | 23             | 3.3                                  | 50 min          | 5 hr        | 7.7                                  | 2.32                                 | 6 hr                         | 6 hr        | 0.29                                 | 3.8                          | 1.15                         | 0.71                                 |
| Homatropine    | 7              | 3.4                                  | 40 min          | 25 min      | 5.9                                  | 1.72                                 | 6 hr                         | 1 hr        | 0.33                                 | 3.3                          | 0.97                         | 1.0                                  |

In the table are given the number of eyes treated with each drug, the times required for maximum mydriasis and maximum cycloplegia, the initial and maximum pupillary diameters, the maximum ratios of pupillary diameters, the minimum remaining fractions of accommodation, the times to onset of recovery from mydriasis and cycloplegia and the observations on diameter of the pupil and residual accommodation made on the fifth day

The table shows that the times to maximum mydriasis were approximately the same for the three drugs but that times for recovery were in

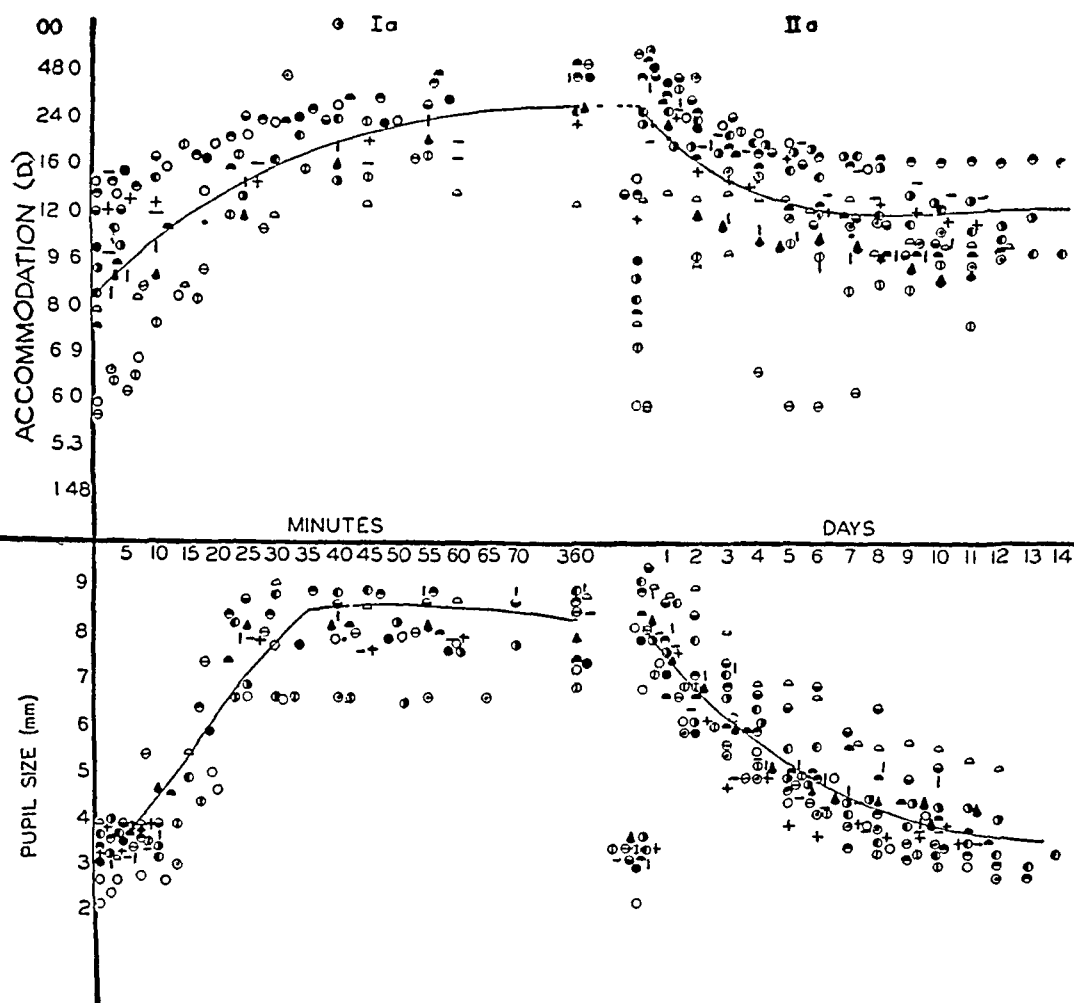


Fig 2—Changes in time of accommodation and of pupillary size after administration of 1 drop of 1 per cent solution of atropine sulfate. During the first hour readings were made at short intervals. Additional readings were made at six hours and thereafter, up to fourteen days. Accommodation is plotted as units  $100/D_t$ , where  $D_t$  is the number of diopters of accommodation at any time,  $t$ .

the following order: homatropine < methylatropine < atropine. Homatropine had a less dilating effect than either methylatropine or atropine.

Homatropine had a considerably more rapid action in producing maximum cycloplegia than did either methylatropine or atropine. Again, homatropine was less potent than the other two drugs, and methyl-

atropine had somewhat less effect than atropine. The recovery from the cycloplegic effects of homatropine was more rapid than that from the effects of methylatropine or atropine. Paralysis of accommodation from methylatropine began to disappear more quickly than that from atropine, but the speeds of recovery were not markedly different for the two drugs.

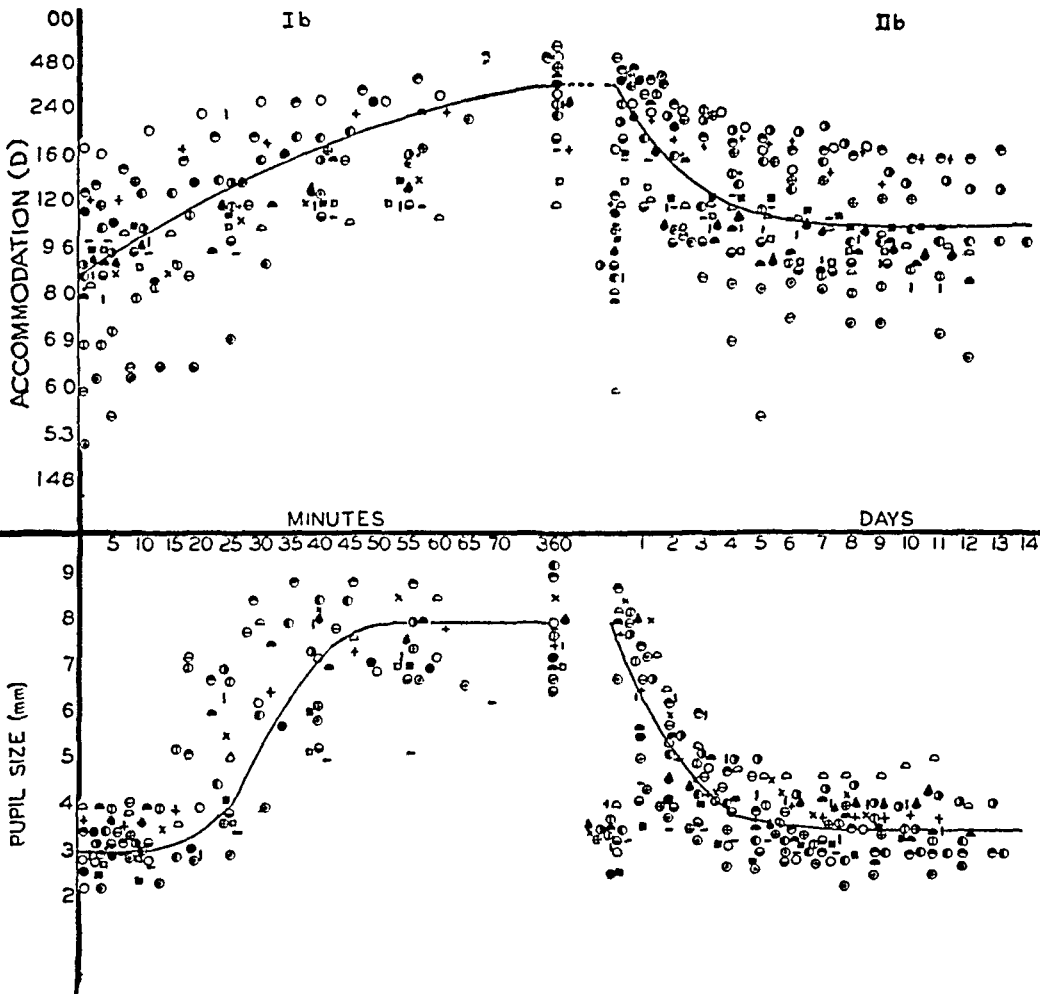


Fig 3—Changes in time of accommodation and pupillary size following the administration of 1 drop of 1 per cent of solution of methylatropine nitrate. See legend of figure 2.

#### COMMENT

This work demonstrates that the effects of atropine, methylatropine and homatropine on the size of the pupil and the accommodating ability of the eye are essentially similar, the chief difference is in the degree of activity. An inspection of figures 2, 3 and 4 shows that for each drug there was a wide variation in response of subjects.

The maximum diameters of the pupils of 8.3 and 7.7 mm for atropine and methylatropine, respectively, are significantly different by the *t* test (Fisher<sup>13</sup>) (*p* is less than 0.01). Thus, it is seen that both homatropine and methylatropine had weaker actions in producing dilation of pupils than did atropine. The speeds with which the three drugs produced their maximum effects were roughly the same, and the speeds of recovery from the mydriatic effects of methylatropine and

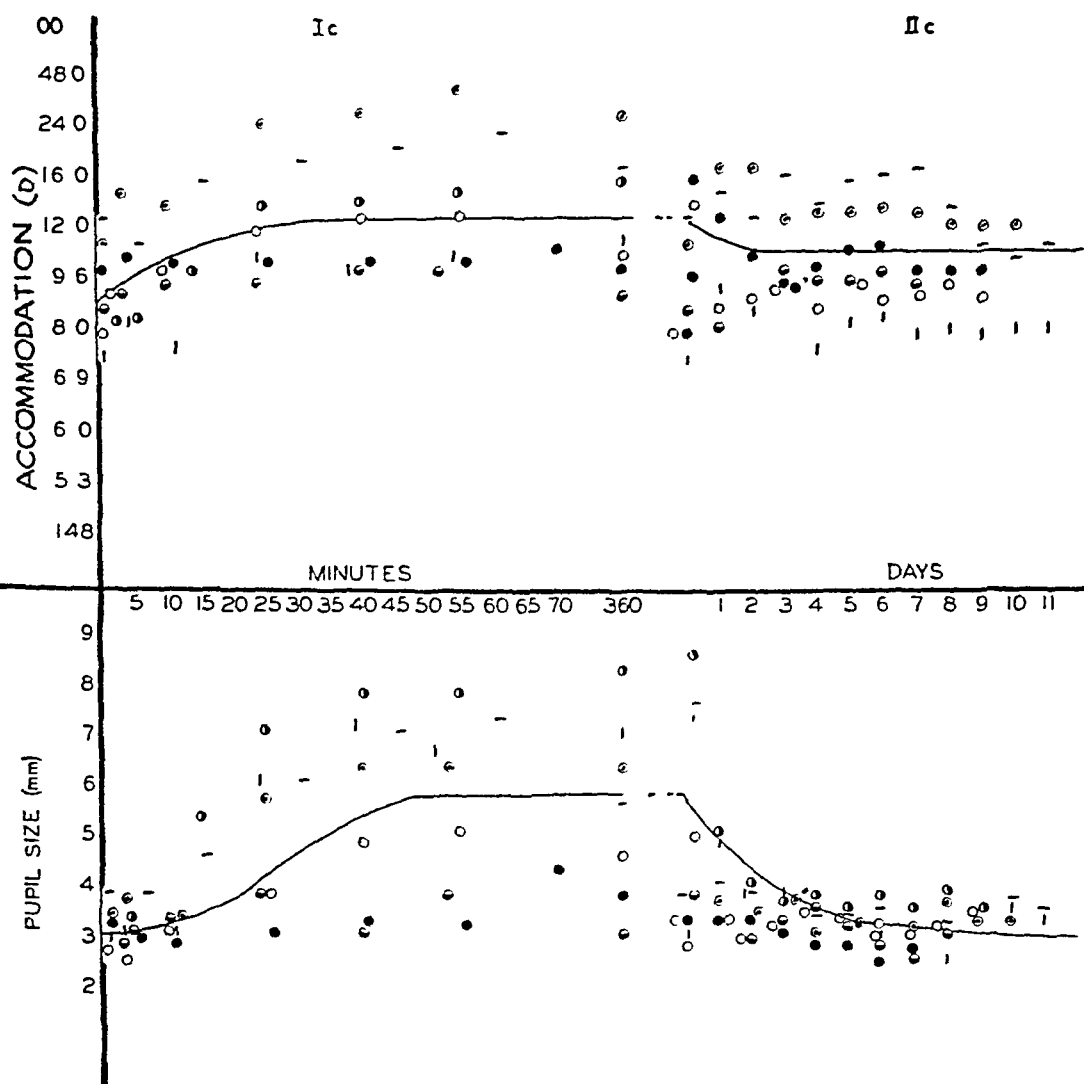


Fig 4—Changes in time of accommodation and of pupillary size following the administration of 1 drop of 1 per cent solution of homatropine hydrobromide. See legend of figure 2.

homatropine were significantly less than the speed of recovery from atropine.

The amount of cycloplegia produced by homatropine was significantly less than that produced by comparable doses of atropine or

13 Fisher, R. A. Statistical Methods for Research Workers, ed 9, London, Oliver & Boyd, Ltd, 1944.



methyلاتropine The time required for maximum effect with homatropine was approximately one-twelfth that required by the other drugs. However, inspection of figure 5 shows that the three curves of loss of accommodation ran roughly parallel during the first few minutes after instillation of the drugs into the eyes. This would make it seem possible that the short time required for homatropine to produce its maximum effect, as compared with the time required for the other two drugs, may be correlated with the weakness of the action of homatro-

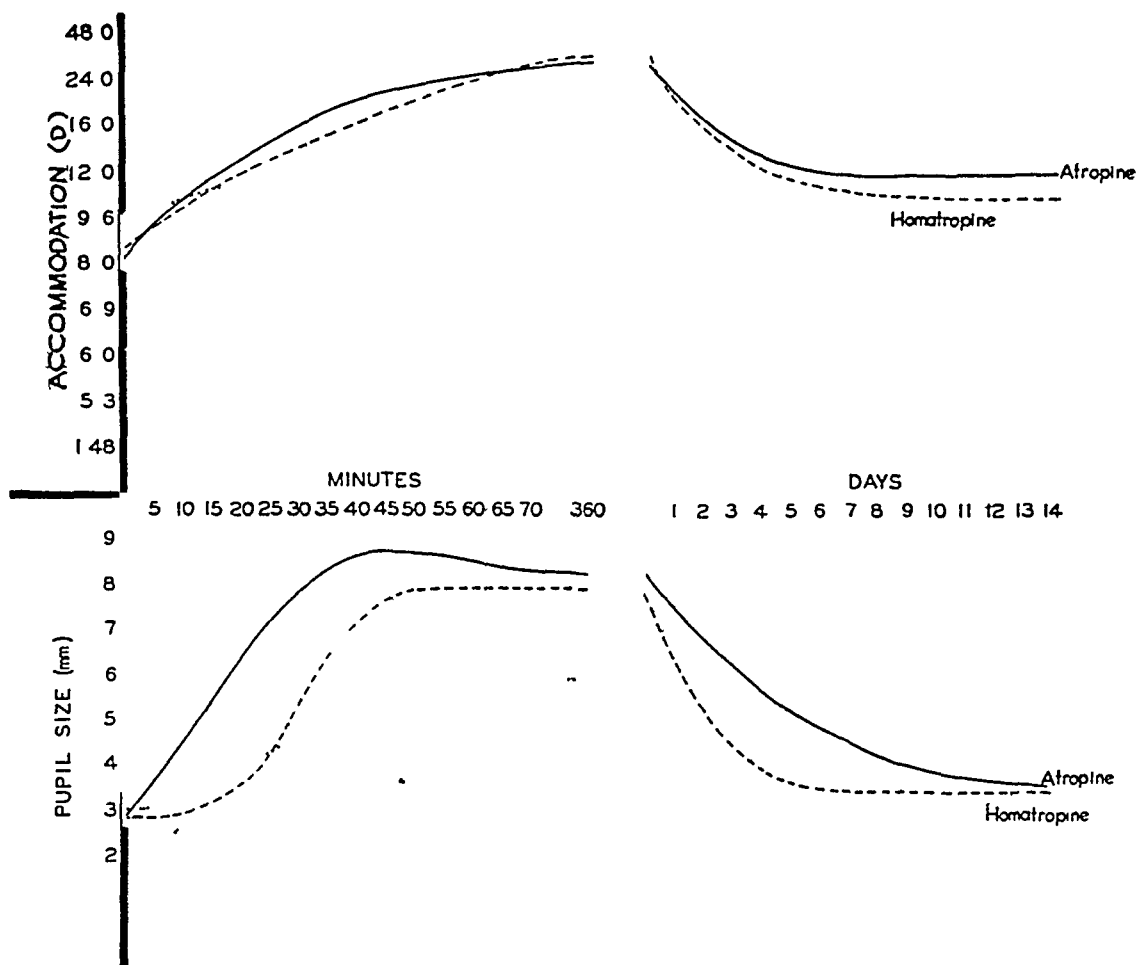


Fig 5—Average curves of changes in time of accommodation and of pupillary size following the administration of 1 drop of 1 per cent solutions of atropine sulfate, methyلاتropine nitrate and homatropine hydrobromide. See legend of figure 2.

pine. Similarly, the relatively more rapid recovery from the homatropine cycloplegia may also, in part at least, be explained by the weak effect of the drug.

While methyلاتropine produced approximately the same amount of paralysis of accommodation as the same dose of atropine, and in approximately the same time, the time for recovery from methyلاتropine

( $68 \pm 38$  days) was possibly somewhat shorter than that for atropine ( $92 \pm 36$  days). The difference is not significant by the *t* test. The fact that methylatropine produced as much cycloplegia and almost as much mydriasis as atropine, and may have permitted somewhat earlier recovery of these two ocular functions, suggests that methylatropine might be a suitable substitute for atropine in ophthalmic practice. As suggested by Goldberg,<sup>9</sup> it might be particularly advantageous for use in children, in whom homatropine usually has an unsatisfactory action. It appears that methylatropine would permit about as easy refraction as atropine and might allow somewhat faster recovery of normal ocular functions.

#### SUMMARY

Atropine sulfate, methylatropine nitrate or homatropine hydrobromide was instilled in equal amounts into human eyes.

Under these conditions homatropine had less mydriatic and cycloplegic effect than either of the other two drugs, and recovery from its effects was the most rapid.

Methylatropine nitrate had significantly less mydriatic action than atropine. The cycloplegic action was about the same as that of atropine.

Dr. J. H. Wills, Jr., gave assistance in this study.

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## NIGHT VISION

### II A Comparison and Critique of Various Procedures Used for Night Vision Testing

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**I**N A previous article<sup>1</sup> comparative data on the results of examination of night vision of 217 Caucasian and 217 Japanese students were reported. The purpose of the present paper is to furnish statistical data on the correlation that was found between the instruments used, to describe briefly some of the other instruments and technics employed in night vision testing and to proffer a plan, based on physiologic and optical principles, for universal adoption for the complete examination of the function of night vision.

#### COMPARISON OF FIVE INSTRUMENTS

The instruments used in the previous survey included the Hecht-Shlaer adaptometer, the S A M Night Vision Tester, the Luckiesh-Moss Low Contrast Test Chart, the Harman Disc Spotting Device and the Ferree-Rand Projectochart. Of the results obtained with these instruments, the figures obtained on the Hecht-Shlaer adaptometer, for the examination of the light threshold, and the scores achieved on the S A M Night Vision Tester were chosen for purposes of comparison with the data obtained with all the other devices.

The accompanying tables are statistical compilations of the responses obtained from the entire group (434 subjects) on all the instruments used during these examinations, appearing in contrast with the two arbitrarily selected standards. In both tables, the subjects were assigned superior, satisfactory or unsatisfactory ratings. The bases of these groupings appear at the head of each column in both tables. It should be noted that in tests with the Hecht-Shlaer adaptometer only those subjects were given superior scores whose light thresholds did not exceed 2.2 log units. This is a slight departure from previous methods of scoring and was done only for the purpose of obtaining a more accurate statistical analysis.

Inspection of the data compiled in tables 1 and 2 shows that though there is some correlation between the responses obtained on the various instruments this is by no means uniform and consistent. Yet the tests

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<sup>1</sup> Holmes, W J. Night Vision. I. Comparison of the Scotopic Visual Ratings of Young Japanese and Caucasian Adults Living in Hawaii, *Arch Ophth* 36:141 (Aug) 1946.

were carried out by the same examiner, using the same technic on subjects of the same age and of approximately the same level of intelligence. This would suggest that either the instruments were at fault or that dissimilar retinal functions were tested, which do not lend themselves to purposes of comparison. Apparently, both these assumptions are at least partially correct. To illustrate. On the Hecht-Shlaer adaptometer, 153 subjects were rated as superior on the basis

TABLE 1—*Correlation of the Results of Examinations for Night Vision of 434 Subjects Obtained on the S A M Night Vision Tester with Scores in Other Tests*

|   | Scores on S A M Night Vision Tester |                               |                                 | Total |
|---|-------------------------------------|-------------------------------|---------------------------------|-------|
|   | Superior<br>(8 and 9)               | Satis-<br>factory<br>(5 to 7) | Unsatis-<br>factory<br>(0 to 4) |       |
| No. of Subjects   | 50                                  | 310                           | 74                              | 434   |
| Hecht Shlaer adaptometer  |                                     |                               |                                 |       |
| Light thresholds (log units)                                    |                                     |                               |                                 |       |
| 15 to 29  | 50                                  | 249                           | 51                              | 350   |
| 30 to 39  |                                     | 50                            | 22                              | 72    |
| 40 and above  |                                     | 11                            | 1                               | 12    |
| Form thresholds (log units)                                     |                                     |                               |                                 |       |
| 25 to 39  | 47                                  | 249                           | 38                              | 334   |
| 40 to 49  | 3                                   | 50                            | 24                              | 77    |
| 50 and above  |                                     | 11                            | 12                              | 23    |
| Disc Spotting Test (Harman)                                     |                                     |                               |                                 |       |
| At distances of 10' to 9'                                       | 40                                  | 140                           | 16                              | 196   |
| 8' to 7'  | 4                                   | 85                            | 28                              | 117   |
| 6' to 5'  | 5                                   | 71                            | 23                              | 99    |
| 4' or less  | 1                                   | 14                            | 7                               | 22    |
| Ferree Rand Projectochart equipped with neutral filter and with |                                     |                               |                                 |       |
| Shutter fully closed  | 41                                  | 147                           | 13                              | 201   |
| Shutter open to 0.25  | 6                                   | 141                           | 50                              | 197   |
| Shutter open to 0.33  | 3                                   | 13                            | 10                              | 26    |
| Shutter open to 0.50  |                                     | 9                             | 1                               | 10    |
| Shutter open to 0.75  |                                     |                               |                                 |       |
| Luckles Moss Low Contrast Test Chart                            |                                     |                               |                                 |       |
| At 10', read lines 20 and 19                                    | 12                                  | 35                            | 5                               | 52    |
| At 10', read lines 18 and 17                                    | 8                                   | 50                            | 4                               | 62    |
| At 10', read lines 16 and 15                                    | 4                                   | 23                            | 2                               | 34    |
| At 10', read lines 14 or less                                   | 15                                  | 26                            | 3                               | 44    |
| At 9', read line 20   | 4                                   | 45                            | 7                               | 56    |
| At 8', read line 20   | 1                                   | 48                            | 15                              | 64    |
| At 7', read line 20   | 3                                   | 28                            | 15                              | 46    |
| At 6', read line 20   | 2                                   | 28                            | 8                               | 38    |
| At 5', or less read line 20                                     | 1                                   | 22                            | 15                              | 38    |

of their low light threshold levels, on the S A M Night Vision Tester only 50 subjects were given superior scores. Thus, on a cursory examination it would seem that there is little, if any, correlation between the results obtained with the two procedures. However, on closer scrutiny one finds that in one test the measurements involved the light threshold and in the other the form threshold. In one procedure the time element was a known, standard factor, while in the other it changed with every click of the shutter.

#### OTHER TESTING TECHNIQUES

As a further illustration, in order to emphasize that dissimilar technics may be responsible for incongruous results, a brief description

of various instruments frequently mentioned in the literature is given as follows

Device 9-B-4, a radium plaque adaptometer, is used for the determination of the form threshold at a distance of 5 feet (1.5 meters). The background is a luminous radium plaque, on which the test object, consisting of the letter T, may be rotated in four different meridians

TABLE 2—*Correlation of the Results of Examination for Night Vision of 434 Subjects by Five Different Methods and Comparison with Measurements of Their Light Thresholds as Expressed on the Hecht-Shlaer Adaptometer*

|   | Light Threshold (log units) Obtained on Hecht Shlaer Adaptometer |                              |                                   | Total |
|---|--|------------------------------|-----------------------------------|-------|
|   | Superior<br>(1.5 to 2.2)   | Satisfactory<br>(2.3 to 2.9) | Unsatisfactory<br>(3.0 and Above) |       |
| No. of Subjects   | 153  | 224                          | 57                                | 434   |
| S. A. M. Night Vision Tester                                |  |                              |                                   |       |
| Lightest filter 0 to 4                                      | 6  | 74                           | 23                                | 103   |
| 5   | 12   | 52                           | 21                                | 85    |
| 6   | 48   | 28                           | 10                                | 86    |
| 7   | 56   | 20                           | 3                                 | 79    |
| 8   | 27   | 41                           |                                   | 68    |
| Darkest filter 9  | 4  | 9                            |                                   | 13    |
| Hecht Shlaer adaptometer form threshold (log units)         |  |                              |                                   |       |
| 2.5 to 3.9  | 143  | 124                          | 14                                | 281   |
| 4.0 to 4.9  | 8  | 77                           | 25                                | 110   |
| 5.0 and over  | 2  | 23                           | 18                                | 43    |
| Disc Spotting Test (Harman)                                 |  |                              |                                   |       |
| At distances of 10 to 9'                                    | 93   | 93                           | 11                                | 196   |
| 8' to 7'  | 43   | 61                           | 13                                | 117   |
| 6' to 5'  | 9  | 60                           | 30                                | 99    |
| 4' or less  | 9  | 10                           | 3                                 | 22    |
| Ferree Rand Projectochart equipped with neutral filter with |  |                              |                                   |       |
| Shutter fully closed  | 97   | 95                           | 9                                 | 201   |
| and   |  |                              |                                   |       |
| Shutter open to 0.25  | 43   | 114                          | 40                                | 197   |
| Shutter open to 0.33  | 11   | 10                           | 5                                 | 26    |
| Shutter open to 0.50  | 2  | 5                            | 3                                 | 10    |
| Shutter open to 0.75  |  |                              |                                   |       |
| Luckiesh Moss Low Contrast Chart                            |  |                              |                                   |       |
| At 10', read lines 20 and 19                                | 28   | 19                           | 5                                 | 52    |
| At 10', read lines 18 and 17                                | 31   | 28                           | 3                                 | 62    |
| At 10', read lines 16 and 15                                | 20   | 13                           | 1                                 | 34    |
| At 10', read lines 14 or less                               | 32   | 11                           | 1                                 | 44    |
| At 9', read line 20   | 14   | 38                           | 4                                 | 56    |
| At 8', read line 20   | 9  | 48                           | 7                                 | 64    |
| At 7', read line 20   | 4  | 29                           | 13                                | 46    |
| At 6', read line 20   | 6  | 20                           | 12                                | 38    |
| At 5', or less read line 20                                 | 9  | 18                           | 11                                | 38    |

The A. A. F. Eastman Night Vision Tester likewise measures the form threshold. The test object is a 1 degree Landolt C. The highest level of intensity for the apparatus is 6.25 micromicrolamberts.

An adaptometer described by Riddell<sup>2</sup> consists in a modification of the Birch-Hirschfeld instrument and is so designed that a relatively constant portion of the retina is tested in an area where there is an approximately equal distribution of rods and cones.

2 Riddell, W. J. B. On Testing Dark Adaptation, Glasgow M. J. **139** 149-157 (June) 1943.

The Koch adaptometer<sup>3</sup> is a modification of the Hecht instrument. The light source in this apparatus is a 25 watt bulb. The light is passed through several filters and graduated to a range of 2 to 6 micromillilamberts by two variables, the diaphragmatic aperture and the speed of a compur shutter. There are fixation points, consisting of radium salt, for either eye so placed that the light falls on the retina 6 degrees from the fovea. For testing form sense a 10 mm rotating E is used, which is placed 380 mm from the patient's eyes. Each eye is tested separately.

Solandt and Best,<sup>4</sup> in Canada, have used another modification of the Hecht-Shlaer apparatus. They reported variations on successive examinations which range from 0.06 to 0.17 log units and concluded that the instrument in their hands has been of value in furnishing consistent results.

Yudkin, Robertson and Yudkin<sup>5</sup> used an instrument modified from the Crookes adaptometer. Their technic consists in adapting the subject to light and then measuring the retinal thresholds repeatedly over a period of forty minutes. They stressed the importance of evaluating dark adaptation in terms of entire function, that is, the cone threshold, the rod threshold, the transition time between the two phases and the final rod threshold level. They expressed the belief that adaptometers which measure the visual threshold only at one particular time are misleading and in many cases erroneous.

An instrument which has gained wide acceptance in the British army is the rotating pentagon<sup>6</sup>. The test object in this apparatus is a large V mounted in five different positions on a translucent screen, illuminated by a small bulb run from a dry battery and controlled by a rheostat and a voltmeter. The lamp is situated at varying distances from each of the five screens. The test is performed in a darkened hut, with the subject seated at a distance of 1 meter from the instrument.

A test has been devised by Metcalfe<sup>7</sup> based on the fact that after exposure to glare preception of green is the last color to return to normal.

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3 Michaelson, I C. Defective Night Vision Among Soldiers. Dark Adaptation Results and Their Use in Diagnosis, *Brit J Ophth* **28** 140-147 (March) 1944

4 Solandt, D Y, and Best, C H. Night Vision, *Canad M A J* **49** 17-21 (July) 1943

5 Yudkin, J, Robertson, G W, and Yudkin, S. Vitamin A and Dark Adaptation, *Lancet* **2** 10-13 (July) 1943

6 Rycroft, B W. Night Vision in the Army, *Brit M J* **2** 576-577 (Nov 14) 1942

7 Metcalfe, E E. A New Method for Determining Night Blindness. Preliminary Report, *U S Nav M Bull* **38** 231-239 (April) 1940

Much has been written about the biophotometer. As recently as May 1944, Schonberg<sup>8</sup> stated that he found the biophotometer invaluable in cases in which vitamin A deficiency has been suspected and as an aid in diagnosis of those conditions in which night blindness is one of the symptoms. However, Oldham and his associates<sup>9</sup> reported that the relationship between the readings in the biophotometer test and the nutritional status with respect to vitamin A was not close enough to warrant the continued use of this test as a means of diagnosing sub-clinical vitamin A deficiencies.

Saubermann<sup>10</sup> studied the power of discriminating differences in luminosity by means of an apparatus on which colored disks can be rotated. In an outer circular portion a colored ring is exposed for comparison with brightness of an inner circular disk, in which the relative quantities of white and black can be changed, using rotation. Differences in luminosity are reported to be less easily perceived as dark adaptation increases.

An instrument called the umbralometer has been described by Costi Garcia de Tunon<sup>11</sup>. This apparatus consists of a 4 volt lamp, a battery with variable resistance, a collimator and a pair of Nicol prisms. By rotation, the Nicol prisms serve as means of obscuration, the zero point is reached when there is complete crossing of the prisms. The advantages claimed for this device are the continuous control of the intensity of the current and of the mechanism of obscuration, elimination of the factor of accommodation, the possibility of making observations in the presence of low visual acuity and the basing of the measurements not on light perception but on the "minimum perceptible," which affords greater sensitivity and greater rapidity of investigation.

The Sloan perimetric light sense tester has been described in a previous article<sup>12</sup>. It is based on determination of the light threshold in several meridians of the visual field from center to periphery.

Davis<sup>13</sup> described a rough test for night vision testing as follows:

Mount on a post at the end of a level space 5 yards wide and 40 yards long and away from all artificial light, a black target on which is a movable white

8 Schonberg, A. L. Plans for Inexpensive Improved Biophotometer, *Mil Surgeon* **94** 308-311 (May) 1944

9 Oldham, H., Roberts, L. J., MacLennan, K., and Schlutz, F. W. Dark Adaptation of Children in Relation to Dietary Levels of Vitamin A, *J. Pediatr* **20** 740-752 (July) 1942

10 Saubermann, G. V. C. Ueber die Unterschiedsempfindlichkeit des dunkel-adaptierten Auges, *Ophthalmologica* **104** 157-165 (Sept.) 1942

11 Costi Garcia de Tunon, C. Presentation of a New Umbralometer, *Arch Soc oftal hispano-am* **1** 114-122 (July) 1942

12 Holmes, W. J. Night Vision, *Arch Ophth* **30** 267-277 (Aug.) 1943

13 Davis, W. T. Military Ophthalmology, *Am J Ophth* **27** 26-44 (Jan) 1944

strip, 6 by 24 inches. Mark off distances from the target at 5-yard intervals. After the person to be tested has been kept away from all artificial illumination for 25 minutes, direct him to walk slowly from the far end of the test area toward the target. The distance at which he is first able to identify correctly the position of the white strip is noted. While the person being tested is walking back for another trial, the white strip is changed. Several trials are made.

It is recommended that this test be performed on a dark night, before the moon has appeared.

Additional tests of dubious scientific, but possibly of some practical, value may be mentioned.

The "scratch test" consists in recording the number of scratch marks on the body of a subject who has hiked through a thick brush of cactus on a narrow, winding lane on a dark, moonless night.

The "self-preservation" test assesses the ability of a subject to emerge relatively unscathed after he has taken part in a game played with a heavy white medicine ball in a completely darkened gymnasium.

The "purgation test" is administered to persons who are suspected of malingering. A strong cathartic is administered in the evening and is so timed that a subject who reported inability to see clearly one night may, without his knowledge, be observed as he rushes for the toilet the next night, after taking the cathartic.

The "latrine test" consists in ordering suspected malingerers to cross in the dark a latrine trench across which a single plank has been laid. If the subject falls in, his disability is considered genuine.

Numerous attempts have been made to correlate vitamin A levels of the blood with the results of dark adaptation. Haig and Patek<sup>14</sup> found no correlation between vitamin A levels of the plasma and the parameters of dark adaptation in normal patients or in patients with cirrhosis of the liver. Steven,<sup>15</sup> however, reported that he found a high degree of correlation between the rise of visual thresholds and the fall of vitamin A levels of the blood. In a study of the amount of vitamin A in the blood and of the visual threshold measured with the Hecht-Shlaer adaptometer, Yarbrough and Dann<sup>16</sup> concluded that a single measurement of the visual threshold is not a reliable indicator of the vitamin

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<sup>14</sup> Haig, C., and Patek, A. J., Jr. The Relation Between Dark Adaptation and the Level of Vitamin A in the Blood, *J. Clin. Investigation* **21**:377-383 (July) 1942.

<sup>15</sup> Steven, D. M. Experimental Human Vitamin A Deficiency. The Relation Between Dark Adaptation and Blood Vitamin A, *Tr. Ophth. Soc. U. Kingdom* **62**:259-275, 1942.

<sup>16</sup> Yarbrough, M. D., and Dann, W. J. Dark Adaptometer and Blood Vitamin A Measurements in a North Carolina Nutrition Survey, *J. Nutrition* **22**:597-607 (Dec) 1941.



A content of the blood Bodansky, Lewis and Haig<sup>17</sup> found that estimations of the vitamin A concentrations of the plasma were considerably more sensitive than tests for dark adaptation in the detection of deficiencies of vitamin A. However, they stated that occasionally abnormal values for dark adaptation are accompanied with normal vitamin A levels of the blood.

In addition to the work already cited, there is a voluminous Russian and German literature on the manifold methods of testing dark adaptation and night vision. The more recent German reports<sup>18</sup> contain repeated references to objective means of examination based on the phenomenon of optokinetic nystagmus. No details, however, are available of the technics that are employed.

An appraisal of these instruments leads to the conclusion that they are not sufficiently interchangeable or mechanically perfected to serve as diagnostic indexes for the assessment of a subject's total night visual capacity.

#### OBJECTIONS TO PRESENT METHOD OF TESTING

The chief shortcomings of the instruments described may be listed as follows. Many measure only the light threshold, and not the form threshold, on the other hand, others express only the form threshold giving no indication of the light threshold. The tests for the most part are conducted in only one area of the visual field, rather than in several areas. The targets for the measurement of form threshold in most of the instruments are of one standard size, rather than of several graded sizes. The duration of stimulation of the retina is controlled in only a few instruments, and then only at one speed, rather than at several speeds. Central fixation is provided for in some of the instruments and left out entirely in others. Perception of colors is considered of great importance in some of the tests, and indeed forms the basis on which the particular machines were constructed but is excluded entirely from others. Some of the examinations are performed monocularly, others binocularly. The distances at which the instruments are placed from the eyes vary all the way from 14 inches (35.5 cm) to 40 yards (36.5 meters).

The principal reason for this apparent confusion is the lack of agreement among investigators as to the real nature of the function to be tested and the even greater lack of uniformity regarding the proper means of testing it.

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17 Bodansky, O., Lewis, J. M., and Haig, C. The Comparative Value of the Blood Plasma Vitamin A Concentration and the Dark Adaptation as a Criterion of Vitamin A Deficiency, *Science* **94** 370-371 (Oct. 17) 1941.

18 Rieken, H., cited by Ohm, J. Adaptationsprüfung mittels des optokinetischen Nystagmus bei Augenzittern der Bergleute, *Arch f Ophth* **145** 31-45, 1942.

The scientific approach to these controversial issues must emanate from the fundamental concepts of anatomy, physiology and optics which govern night vision

#### PHYSIOLOGIC CONSIDERATIONS

Even at the risk of being pedantic, the terms, "dark adaptation" and "night vision" are redefined, as their improper interpretation has frequently been responsible for erroneous deductions. Dark adaptation refers to the increase in the sensitivity of the eyes that occurs when one passes from bright light to darkness. Night vision constitutes the visual sensation that takes place when the eyes are already in a relatively high state of dark adaptation. Thus it becomes obvious that the two functions are not synonymous and that tests for one cannot be used as diagnostic indexes for the other. This statement has been corroborated by Behr,<sup>19</sup> Best<sup>20</sup> and Wessely,<sup>21</sup> who found no abnormalities in the course and end values of dark adaptation in clinically pronounced cases of night blindness. Birnbacher,<sup>22</sup> similarly, concluded that tests for dark adaptation were not sufficiently indicative to serve as a basis of judgement of the extent of impairment of night visual function.

Whether the tests should be carried out monocularly or binocularly has been answered by Allen,<sup>23</sup> who found that shading one eye depressed the sensitivity throughout the spectrum not only of the other eye but of the rest of the retina of the same eye, the maximum effect being obtained not in complete dark adaptation but with very dim light. Schumacher<sup>24</sup> further stated that only the dark apparatus has the faculty of summation of impressions of both eyes. An anatomic background for these conclusions was discovered by Frey,<sup>25</sup> who found centrifugal neural paths

19 Behr, C. Das Verhalten und die diagnostische Bedeutung der Dunkeladaptation bei den verschiedenen Erkrankungen des Sehnervenstammes, *Klin Monatsbl f Augenh* **5** 193 and 449, 1915

20 Best, F. Demonstrationen zur Funktionprüfung des Auges, *Ber u d Versamml d deutsch ophth Gesellsch* **3** 201-204, 1918

21 Wessely, K. Ueber Störungen der Adaptation, *Arch f Augenh* **81** 53, 1916

22 Birnbacher, T. Die epidemische Mangelhemeralopie, *Abhandl a d Augenh u Grenzgeb*, 1927, no 53, pp 18-19

23 Allen, cited by Duke-Elder, W. S. *Text-Book of Ophthalmology*, St Louis, C. V. Mosby Company, 1937, vol 1, p 952

24 Schumacher, G. Ueber das Verhalten der monokularen und binokularen Reizschwelle während der Dunkeladaptation des Tages- und Dämmerungsapparates, *Acta ophth* **15** 5-59, 1937

25 Frey, E. Vergleichend-anatomische Untersuchungen über die basale optische Wurzel, die Commissura transversa Gudden und über eine Verbindung der Netzhaut mit dem vegetativen Gebiet Hypothalamus durch eine "dorsale hypothalamische Wurzel" des Nervus opticus bei Amnioten, *Schweiz Arch f Neurol u Psychiat* **39** 255, 1937, **40** 69, 1937

between the central parts of the brain trunk and the retina. This fact suggests the possibility of a reciprocal relationship between the brain and the retinas of the two eyes and throws additional light on the importance of dark adaptation in the phenomena of contrasts.

The size of the test object in determinations of the form threshold is of great importance. According to recent reports,<sup>26</sup> an average-sized plane cannot be discerned much over 1,000 feet (300 meters) away on a dark night. This corresponds to a 20/400 image. Such an image has to stimulate a considerable number of rods in a fairly large retinal area in order for it to be perceived by the brain. The recognition of smaller objects offers even more of a problem, as it is well known that the rods, unlike the cones, are not connected with individual nerve fibers but are bunched together and produce an indistinct blurred image only by summation of several subliminal stimuli. Nevertheless, for the purpose of qualitative discrimination, it is deemed advisable to conduct tests of the form threshold with several progressively smaller targets.

The retinal area which is most sensitive in the dark-adapted state, and which therefore should receive the greatest attention, extends between 30 and 50 degrees from the fixation point. There is, however, another retinal area of equal importance in measurements conducted at low values of illumination. This is the so-called intermediate, or "transitional, zone," composed chiefly of rods, but also containing cones, and extending between 2 and 3 degrees from the fixation point. It is in this region that the retinal activities pass from the photopic to the scotopic mechanism. The study of this area is of practical significance as it functions at twilight, dusk and dawn, when both the scotopic and the photopic mechanisms may be called into play.

Central fixation is of undoubted value for measurements involving the light and form thresholds in multiple retinal areas at close range. It is also of consequence when the light and form thresholds are contrasted with each other in a definite sector of the retina. Both red light and self-luminous fixation devices may be utilized for this purpose. However, when the test object is large and is placed at considerable distance from the observer's eyes, it would seem more prudent to discard central fixation altogether and encourage the subject to scan the visual field with a series of quick, jerky movements, interrupted by short pauses, than to stare steadily at one or the other side of the object.

Measurements of the form threshold should also be conducted at distances ranging from 3 to 10 feet (0.9 to 3 meters) from the observer, utilizing larger targets.

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26 *The Use of the Eyes at Night*, United States Navy Department, Bureau of Medicine and Surgery, June 1939, pp. 660-665.

According to Michaelson, much valuable information may be gained by the routine investigations of both the light and the form sense. He found that patients with defective night vision have a poor minimum form sense. However, persons without defective night vision may also have a poor minimum form sense. When poor minimum light sense is associated with good minimum form sense, it indicates malingering.

The exact intensity of illumination at night is still a matter of controversy. According to Moon,<sup>27</sup> night vision can be considered to have supervened when the intensity reaches about 0.001 millilambert. For purposes of examination, instruments that furnish illumination ranging from 1 to 6 micromicrolamberts have been found adequate.

#### RECOMMENDED TECHNIC OF EXAMINATION

*Preliminary Procedures*—Before the actual examination of the night visual faculty is undertaken, the following preliminary procedures should be carried out:

- 1 Inquiry into the past and family histories of the patient. This should include questions regarding hereditary and preexisting ocular diseases, previous gastrointestinal and metabolic disturbances, use of alcohol and drugs and all other factors which might have a bearing on the perception, conduction and interpretation of images at low intensities of illumination.

- 2 Determination of the age of the patient. It is well known that with advancing years, owing to senile changes in the lens alone, there are often increased absorption and retarded transmission of radiant energy.

- 3 A psychiatric appraisal of the subject. The importance of the willingness and eagerness to cooperate and an estimate of the reaction time of the nervous system in examinations of the scotopic state cannot be adequately emphasized and has already been alluded to in the first portion of this report. Indeed, the psychiatric examination is of such far reaching clinical significance that until a reliable objective method of testing is devised an impartial evaluation of night vision cannot be accurately made.

- 4 Examination of the photopic visual acuity of each eye for distance, with correction if such is worn. In this regard, it is felt that the patient who wears a correction for distance to improve his photopic vision should keep his glasses on while he is being tested for his scotopic ability. No amount of persuasion will make him believe, especially if he is wearing a strong correction, that his night vision will not be adversely affected by his being tested with his naked eyes. As a matter of strict fact, there is no conclusive experimental evidence that scotopic vision remains entirely

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<sup>27</sup> Moon, P. *The Scientific Basis of Illuminating Engineering*, New York, McGraw-Hill Book Company, Inc., 1936.

unaltered when carried out in the absence of the magnifying or minifying effects of lenses worn during the photopic phase of seeing

5 Careful examination of the external ocular segments, the media and the fundi of both eyes

6 Estimation of the errors of refraction of each eye

7 Preexposure of both eyes to a known intensity of light for a known length of time (e g, to a brightness of 1,500 millilamberts for three minutes)

8 Dark adaptation for thirty minutes This may be accomplished by the use of dark adapter red goggles for twenty-five minutes, followed by a five minute period in a completely darkened room, or, preferably, by staying in a completely dark chamber for the entire thirty minutes

#### THE EXAMINATION PROPER

A systematic examination of a subject's night perception may then be made, according to the following technic

1 Plotting of the entire course of dark adaptation This is to include determination of

- (a) the cone threshold,
- (b) the transition time between the cone and the rod threshold,
- (c) the rod threshold, and
- (d) the final rod threshold level

2 Determinations of the light threshold in at least four quadrants of the visual field, in retinal areas corresponding to 40 degrees from the central fixation object

3 Determinations of the form threshold, in a manner similar to that outlined in 2

4 Correlation of the light and form thresholds The ratio thus obtained should be compared with a predetermined standard and may in some cases aid in the detection of malingering

5 Determinations of the light threshold at several time intervals Speeds of 1, 1/2, 1/5, 1/10, 1/20 and 1/40 second are recommended

6 Determination of the form threshold at the transitional zone of the retina 2 to 3 degrees from the fixation object

7 Determinations of the light threshold throughout at least 1 meridian of the visual field, from center to periphery (according to Sloan's technic)

8 Determination of the form threshold with a series of graded objects, beginning with an object corresponding to the 20/400 letter and substituting smaller objects in the successive tests

9 Examinations conducted out of doors on a starlit, moonless night, according to Davis' technic or one of its modifications

10 Serologic studies of the vitamin A concentrations of the blood plasma

11 Further investigations, if such are indicated, in instances in which additional information is desired by the examiner. The procedures employed in these instances depend entirely on the examiner's ingenuity and on the circumstances bearing on the individual case. A few such tests which have been recommended, and might be put to use if desired, include (*a*) use of a longer adaptation time, (*b*) trial feedings with controlled quantities of vitamins A, B, C, and D, calcium, and placebo substances, (*c*) administration of such substances as oxygen, ephedrine, amphetamine and thyroid, (*d*) retests of night vision after the subject is exposed to a trial series of conditioned reflexes, and (*e*) the "cactus test" and other procedures

12 One or more reexaminations of all subjects who failed on the first test, before their night vision is definitely declared unsatisfactory. Indeed, even subjects with superior abilities should be retested, and the results of the second examination should be recorded, as they are of more value than those of the first examination

It is neither necessary nor desirable to carry out all these tests on every subject or to repeat the entire procedure when a candidate comes up for reexamination. Tests 1 to 6 will in most instances provide sufficient information to enable the examiner to classify his subject correctly as having superior, satisfactory or unsatisfactory night vision. The remaining tests are included for the purpose of providing an orderly method of examination, especially for subjects who possess highly developed night visual capacities and who have to be selected for specialized duties requiring such abilities

During war, a study of the intricate problems of night vision is of practical significance in determinations of the suitability of men for night operations. In peacetime the subject will be of even greater practical importance, as the results of light and form threshold examinations will enable the ophthalmologist to suspect an incipient lesion of the posterior segment of the eye before irreversible changes in the fundus have taken place

The establishment of universally accepted standards for the determination of the factors that constitute a person's ability to see in the dark is extremely desirable. Such a procedure would enable different observers in different parts of the world to accumulate extensive statistical data based on a uniform technic and expressed in uniform terminology and would lead to a better understanding of this important and relatively mis-comprehended phase of ophthalmology

## SUMMARY

Comparisons were made of six devices used for investigating night vision. The correlation that existed among these devices was not sufficient to warrant their use interchangeably. A partial list of additional devices used for testing dark adaptation and night vision is appended, together with objections raised against them. A thorough, systematic method of examination based on physiologic principles for the study of the function of night vision is described and its uniform acceptance advocated.

45 Young Building

## REDUCTION OF REFLECTIONS

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OF ALL the technical advances to come out of the recent war, probably the most significant optically is the coating of lenses with reflection-reducing films. Now that coating has been made available to members of the profession, an appraisal of it is in order, for at present it has both limitations and important uses.

This development had its beginning as far back as 1892, when H. Dennis Taylor, a lens designer of England, observed that the iridescent tarnish which appeared on certain old camera lenses did not



Fig 1—Left half of glass coated to reduce reflection

reduce the light they transmitted, but increased it instead. The thin film<sup>1</sup> on these optical surfaces reduced reflections and increased the transmitted light by the amount of reduction of the reflections.

The physical conditions which produce zero reflection of monochromatic light are two. The film must equal in optical thickness one quarter of a wavelength of the incident light, and the refractive index of the film must be the geometric mean of the indexes of the first and second mediums. Under the most frequently encountered condi-

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From the Department of Research and Education, the Univis Lens Company

<sup>1</sup> The metal oxides had been leached from the surface, leaving a thin layer of high silica glass of low density and, hence, low index of refraction.



tions (air to glass) the index of the intervening film should equal the square root of the index of the glass, and the film should be 0.000004 inch thick. The more nearly these conditions are satisfied, the more completely are reflections damped.

This damping is caused by destructive interference occurring at the two surfaces of the low index film, and, in accordance with the law of conservation of energy, the reduction in reflected energy is added to the transmitted beam.

Taylor developed methods of artificially tarnishing lenses, but the reduction in reflection was slight because the index of the film was not low enough for many glasses and the proper thickness was not appreciated. Other methods of approximating the requisite conditions were developed later, until, prior to the recent war, reflections were reduced by leaching lens surfaces with acids or their vapors, by coating with various stearate films and by whirling lenses so as to spread a thin layer of viscous fluid of low index evenly over the surface by centrifugal force. Some of these methods produced relatively durable surfaces and some relatively efficient ones, but none did both.

Since 1938 Strong, whose work was done at the California Institute of Technology, and Cartwright and Turner, whose major work was done at the Massachusetts Institute of Technology, have developed a process which combines the maximum efficiency with the greatest durability. This process, as utilized in optical lenses for the armed forces of this nation, consists in depositing a thin film of magnesium fluoride on optical surfaces in high vacuum and under considerable heat.

Lenses to be coated are treated with a detergent solution and then cleaned long and rigorously, so that no trace of foreign material or oxide remains on the surface. They are then racked in the top of a bell jar and heated to  $400 \pm F$  while the chamber of the bell jar is exhausted to an extreme vacuum of  $4 \times 10^{-6}$ , mechanical vacuum pumps and a high speed oil diffusion pump being used in series. Less than 1 part of air in 100,000,000 remains. After a protracted period under these conditions, the glass is degassed, and its raw substance is exposed. At this point pure magnesium fluoride, held in a crucible in the bottom of the bell jar, is heated by filaments of such high incandescence that they cannot be viewed with the unprotected eye. Under these conditions of heat and high vacuum, the magnesium fluoride vaporizes, and a molecular spray is deposited on the exposed under surface of the lenses. The technician, using a small fluorescent light source, judges the thickness of the film as it accumulates on the lenses by observing reflections from the surface of a monitor lens. As the deposition begins, the usual bright, white reflections from the lenses begin to dim and turn to a straw color. Then, growing dimmer all the time, they go through a succession of yellows, reds and reddish

blues, until when they reach a specific purplish tint the evaporation is stopped. At this point reflections are dimmed for all wavelengths but most completely dimmed for yellow (the one-quarter wavelength condition is exactly fulfilled for yellow of wavelength 555 millimicrons and less perfectly satisfied as the wavelengths of the other colors of the

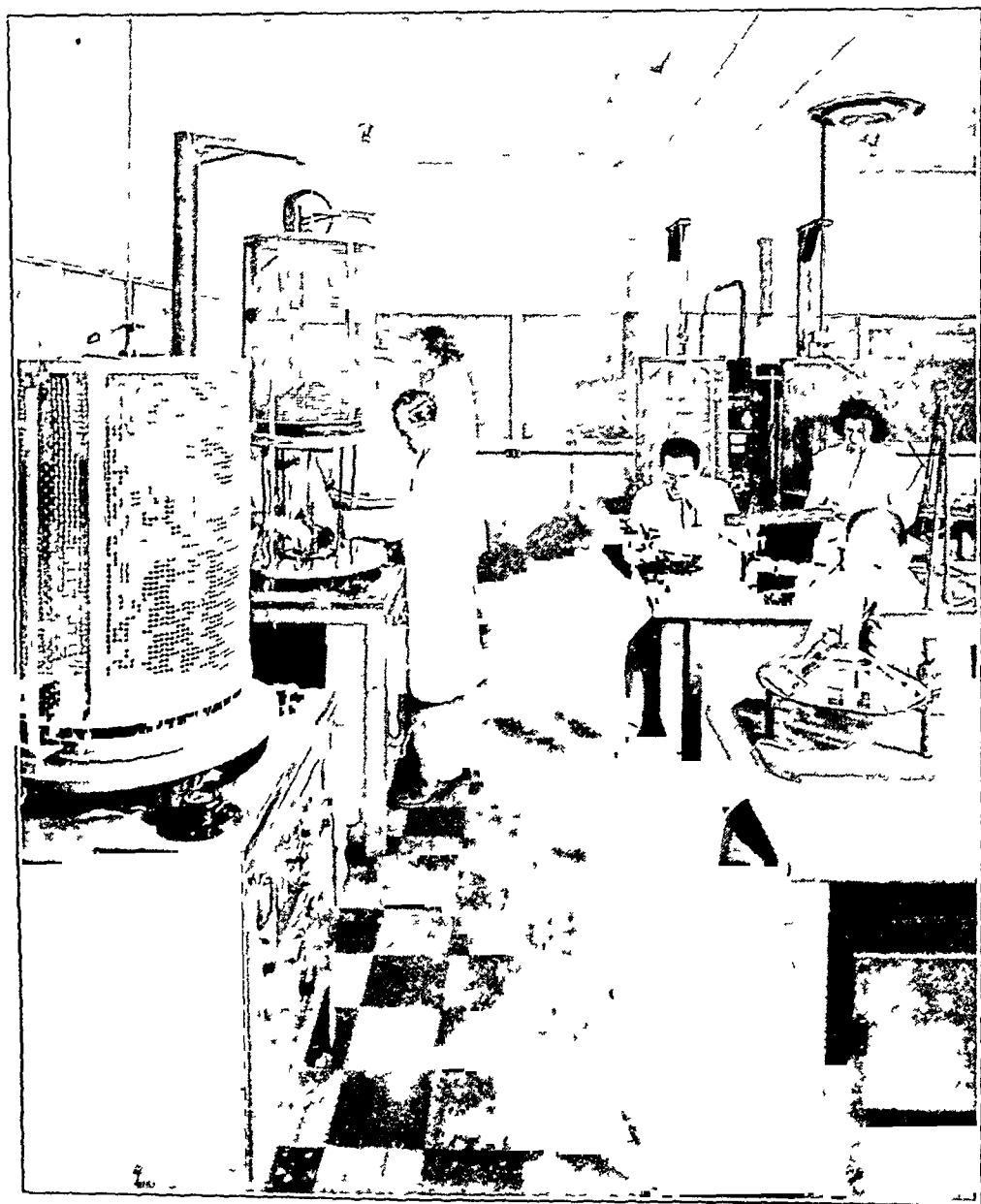


Fig 2—Coating laboratory of the Univis Lens Company in operation

spectrum differ from that of yellow) The slightly greater reflections of wavelengths at the two ends of the spectrum—the reds and violets—when blended produce the purplish tinge characteristic of the residual reflections from coated lenses. This is the condition of maximum reduction of reflections under ordinary daylight. After completion of the deposition the lenses may be baked in vacuum for a considerable

time and then returned slowly to room temperature. The entire operation takes place in a laboratory in which conditions of temperature and relative humidity are controlled, and the air is Preciptron cleaned.

The result is a film almost exactly 0.000004 inch thick, which, when protected in optical instruments, is as permanent as the glass. On crown glass of index 1.52 the film reduces the amount of loss of light at each surface by a factor of 3. The reduction is not greater because magnesium fluoride has too high an index to satisfy perfectly the square root relationship and because in heterogeneous daylight the one-quarter wavelength condition cannot be satisfied for all wavelengths.

When light, traveling in air, impinges on the polished surface of crown glass of index 1.52, the loss is 4.2 per cent at each surface. Coating with magnesium fluoride reduces this loss to 1.3 per cent. In an optical system made up of many surfaces, the cumulative saving in light is considerable. In a regular binocular, consisting of ten optical surfaces, the following differences prevail:

|                                       | Uncoated<br>Lens | Coated<br>Lens |
|---------------------------------------|------------------|----------------|
| Percentage of light absorbed by glass | 12               | 12             |
| Percentage lost by reflections        | 33               | 10             |
| Percentage of light transmitted       | 55               | 78             |

In systems with a greater number of surfaces the gain is even more striking.

The result is, in bright daylight, a reduction of ghost images due to interface reflections, and an increase in contrast and detail. In dim illumination this conservation of light often makes an optical system useful when before coating it would not have transmitted enough light for seeing. The tremendous value of this in extending, both at dusk and at dawn, the period of usefulness of photographic operations, observation devices and gunfire control systems can be appreciated. As a result, during World War II coating became mandatory for practically every optical system used by American fighting men. The creating of laboratories to treat the many millions of optical surfaces required was one of the production phenomena of the war just passed. Procurement of the high vacuum equipment was even permitted to compete with that of high vacuum equipment for the production of uranium 235, used in atomic bombs. In instrument optics, coating is an unqualified success, contributing much improvement, with no disadvantages.

But in ophthalmic optics one finds different and more exacting conditions. As a result one cannot, at this stage of development of the science, expect a repetition of the almost 100 per cent acceptance found in instrument optics. For ophthalmic use the coat must be rugged

indeed, for it is exposed to repeated cleaning and much abrasion. The reduction of reflections is only about 50 per cent, for the incidence of the light varies greatly, so that the one-quarter wavelength condition is not always entirely satisfied, even for yellow light. Scratches on a coated surface are more visible, for the light they reflect is more apparent against a dimly reflecting, coated surface than it would be against a brightly reflecting uncoated one. Furthermore, the gain in transmission, which is so important in a multisurface system, is practically meaningless in a two surface lens, in which loss of light is seldom a problem. Hence the coating of spectacles is of value only to the extent to which it can reduce reflections and at present can be recommended only when reflections are a problem.



Fig 3—Patient with left lens coated for reduction of reflections

Reflections from glasses into the eyes of the wearer occur with every one who wears them. But it cannot be said to constitute a serious problem until the intensity of the reflections exceeds the tolerance of the patient. The intensity of reflections is highest when the prescription is of considerable power or when the wearer is in such a position that a window or bright source is behind and to the side. The tolerance of reflections will be lowest in neurasthenic and hypercritical patients. The result is a fair, though not yet accurately determined, proportion of patients who are consciously annoyed by reflections from their glasses and who are greatly relieved when these are substantially reduced.

This does not mean that the great body of patients who have learned to ignore reflections from their glasses would not welcome a reduction of the reflections, just as one, unconscious of a continuing noise, is relieved when the noise stops. But when coating has been available only for a limited time, a definite assertion to this effect cannot be made.

Reflections from glasses can do more than annoy the wearer. They can, and often do, conceal the eyes of the wearer from any one looking at him. This is detrimental enough in daily personal contacts, when the audience consists of one or a few. But to ministers, teachers and all who wear glasses when appearing before groups of people it is a serious impediment. Their expressions are masked, and the glare, coming and going as the speaker turns, is a disturbing thing to all the audience. Coating will considerably reduce such masking of the eyes.

In summary, it may be said that the coating available today through ophthalmic supply laboratories is durable, if not permanent, and reduces reflections substantially, although it does not extinguish them or make the glasses invisible. Coating is a new and important development which has reached a state of real usefulness, but not of perfection. As such, its judicious employment will increase the ways by which the profession serves and satisfies patients.

Univis Lens Company

## PRESERVATION OF CORNEAL TISSUE FOR TRANSPLANTATION

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WITH the advent of the corneal transplantation operation, there has been a gradual intensification of interest in the donor material to be used for this operation. The institution of the Eye Bank for Sight Restoration to supply adequate material for this operation is a step forward in the right direction, for this organization facilitates a rapid distribution of donor material to the proper place. However, the actual preservation of corneal material involves much more than meets the eye of the casual observer, and there is widespread misconception about this subject.

Contrary to the general opinion, corneal tissue is relatively short lived, and the best operative results in corneal transplantation are obtained when the material is fresh and used shortly after it is removed from the donor. Adult eyes after enucleation show normal transparency and no marked increase in corneal thickness due to edema for forty-eight to seventy-two hours, but thereafter the cornea becomes gradually and progressively edematous, thick and hazy. All these features contraindicate the use of this tissue as favorable donor material. Eyes removed from stillborn infants show more rapid loss of corneal transparency than do adult eyes, and consequently more care must be exercised in evaluating gross changes to determine whether the material is suitable for grafting. I have observed the corneas of stillborn infants become opaque and thick during the course of eighteen hours. The development of these characteristics, of course, foretells failure if such a cornea is used for transplantation. It often is not possible to tell whether corneal tissue is suitable for grafting until it is sectioned with the keratome, for such tissue may appear fairly transparent but on section may be found to have increased in thickness and possess a spongy character that will make it wholly unsuited for use in transplantation.

It was because of these varied problems and the general interest in this subject that a series of eyes were studied to determine the efficacy of various mediums that might be useful in the preservation of corneal tissue. The eyes used for study were obtained from rabbits

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The question was raised as to whether or not the eye should be preserved intact or whether the cornea should be removed and suspended in solution or the fluid of the anterior chamber replaced with the preserving medium

In removing the cornea and suspending it in solution, the difficult problem was encountered of satisfactorily cutting the corneal graft without adequate support. Moreover, corneal tissue rapidly became extremely edematous when suspended in any of the mediums used. A similar condition followed when the anterior chamber was drained and

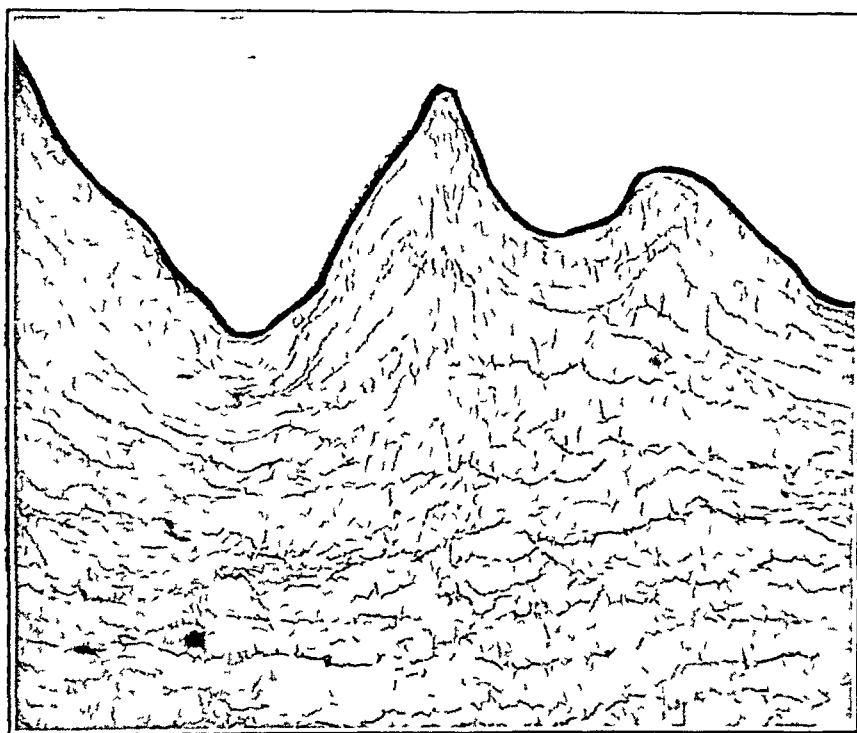


Fig 1—Microscopic section of edematous corneal tissue of an eye in which the fluid of the anterior chamber had been replaced with isotonic solution of sodium chloride and kept two weeks

replaced with the preserving medium. Figure 1 shows a microscopic section of corneal tissue from a rabbit in which the anterior chamber was replaced with saline solution and two weeks was allowed to elapse. A similar thickening took place with all the solutions employed.

The following mediums were used: (1) isotonic solution of sodium chloride, (2) Hartmann's solution, (3) Hartmann's solution and 5 per cent dextrose, (4) plasma, (5) oxygenated plasma, (6) freezing agents, namely, (a) liquid nitrogen and (b) sodium pentothane (isopentane).

## METHOD

The eyes used were removed under strictly antiseptic conditions. They were placed in small tubes containing 5 cc of the preserving medium, this being enough to cover the specimen. These tubes were then kept in refrigeration at 3 C. At the designated times, the eyes were removed and corneal grafts obtained and transplanted to a normal eye.

Bacteriostatic agents were used early during these experiments, but because of the relatively short time the tissue could be kept this precaution was found to be unnecessary.

## RESULTS

*Suspension in Mediums*—Isotonic solution of sodium chloride was an adequate medium for keeping corneal tissue transparent for as long as three days. Uniformly transparent grafts were obtained when tissue was used up to the three day limit (fig 2A). By the fourth or fifth day the cornea was still fairly clear, but sections showed that the tissue was beginning to be spongy and thickened, and microscopic examination showed edema. When this material was used for grafting, the resultant



Fig 2—A, clear corneal graft. Donor material was kept for three days in isotonic solution of sodium chloride. B, corneal graft, showing clear area. Donor material had been kept for five days in isotonic solution of sodium chloride.

transplant in most cases was completely opaque. However, the opacity of this graft was not as thorough or as complete as that of a graft using material kept for one week. The former in most instances showed relatively clear areas, but these were not uniform and were present in only 10 of the 15 specimens studied. The grafts from the remaining 5 corneas had a diffusely hazy character, through which the detail of the fundus could not be seen. In the eyes that showed relatively clear areas of cornea, such as the tissue shown in figure 2B, the fundus could be observed, but the detail could not be clearly made out. Microscopic section of the graft shown in fig 2B revealed diffuse fibrosis which was not present in sections through the clearer area. This fibrosis did not involve all the layers of the cornea, as is apparent in comparing the microscopic pictures in figure 3A and B. It was generally noted at this point that corneas preserved in saline solution were clearer and of more normal thickness than tissue similarly preserved in plasma. A few specimens were kept as long as one month merely to study the



changes taking place in the tissue, and it was found that, although all corneas at this time were greatly thickened and hazy, those preserved in saline solution showed the lesser change from normal

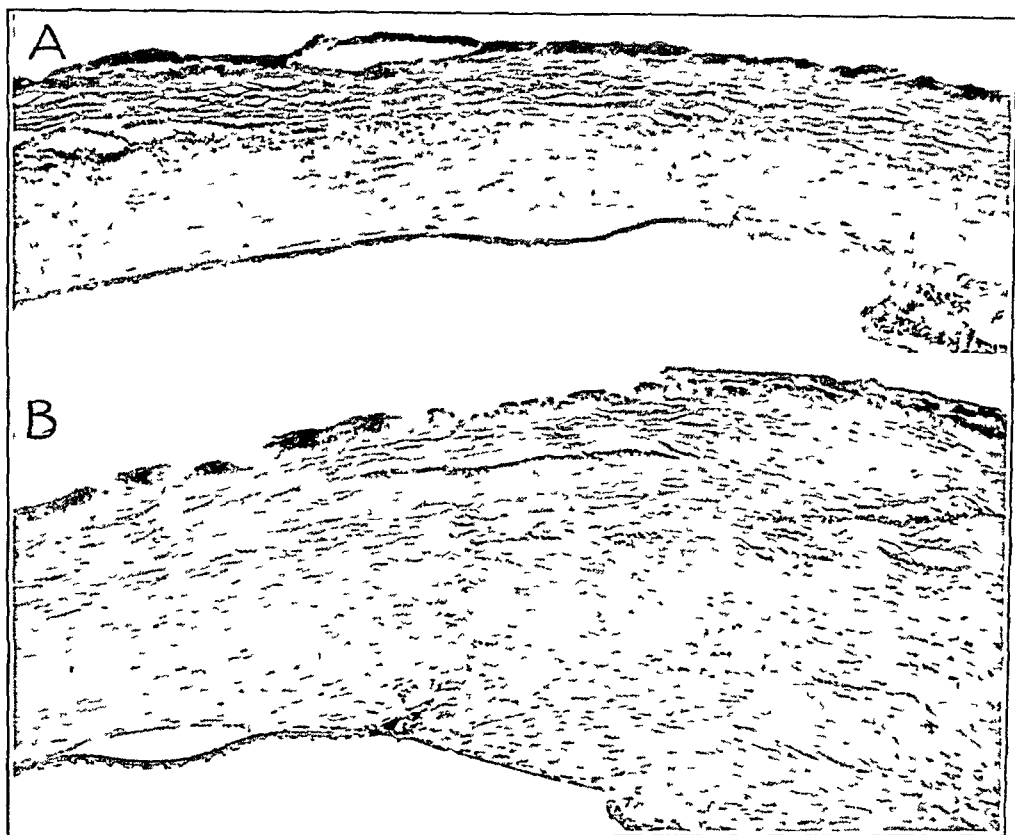


Fig 3—Microscopic sections of the corneal graft shown in figure 2 *B*. *A* is through the clearer area, and *B*, through the opaque area

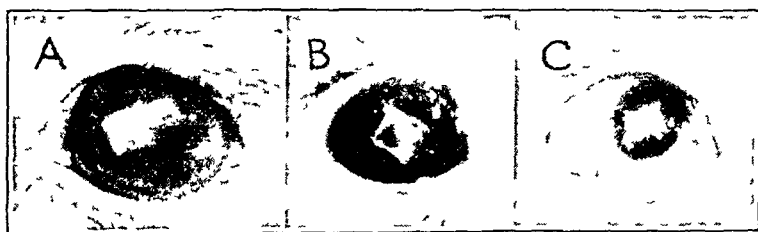


Fig 4—*A*, corneal graft, showing complete opacity. Donor material had been kept for one week in isotonic solution of sodium chloride. *B*, corneal graft, showing diffuse haziness. Donor material had been kept for five days in blood plasma. *C*, opaque corneal graft. Donor material had been kept for one week in blood plasma

In eyes kept for one week the corneas repeatedly showed slight haziness but no great thickening, and when used for transplantation the grafts became completely opaque. The grafts from these eyes appeared to have a uniformly opaque character (fig 4 *A*) and did not show any of

the clearer areas noted in those kept four or five days. In this series, 10 specimens were studied and used for transplants, and all showed the same results. After one week the haziness and thickening progressively increased, so that in two weeks the corneas were wholly unsuitable for grafting. Microscopic examination of this tissue showed pronounced separation of the stromal layers by edema.

Hartmann's solution, used alone or with the addition of 5 per cent dextrose, was a suitable medium for keeping the corneas clear for three to four days, but thereafter they became progressively hazy and thickened. In general, eyes kept in this medium followed the same course as that observed when isotonic solution of sodium chloride was used.

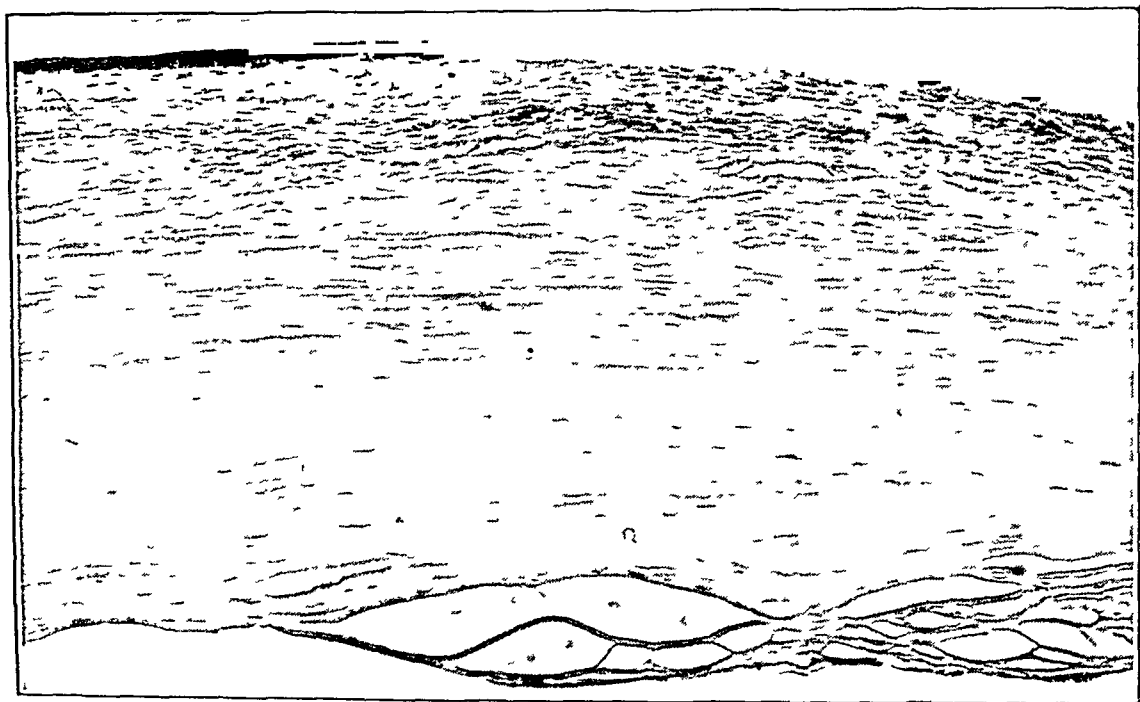


Fig 5—Microscopic section of the opaque corneal graft shown in figure 4 C. There are diffuse infiltration, fibrosis and hyalinization.

Plasma, either alone or oxygenated, was adequate to keep the cornea clear up to a period of three days, but after this time limit the material became useless for transplantation. At the end of four days the cornea began to thicken but still retained a reasonable amount of transparency, and microscopic examination showed edema. Use of this tissue for transplantation resulted in an opaque graft in most cases. Fifteen specimens were studied in this series, and 10 of them were uniformly opaque but, again, the haziness of the graft was not extreme, and no detail of the fundus could be observed (fig 4B). Only in 5 of these specimens were small clearer areas noted. At the end of one week the transparency of the corneas kept in such a medium was not greatly lessened but the tissue was beginning to thicken. Transplantation

A microscopic section of such a graft (fig 5) revealed diffuse fibrosis of all the layers, and showed much denser hyaline and fibrous changes than those seen in figure 3

*Freezing Method*—The freezing experiments were done in collaboration with Dr Arnold Lazarow, of the department of anatomy of Western Reserve University. A small wire mesh container was used to place the eyes in the freezing medium. Liquid nitrogen was the agent used, which lowered the temperature to  $-185^{\circ}\text{C}$ . Eyes placed in this medium were frozen solid in a few seconds. Before the specimens were placed in the freezing solution, a 5 mm trephine opening was made in the sclera, including the optic nerve, to allow for expansion. Otherwise, the cornea would have shown multiple fracture lines when the tissue returned to normal temperature. One series was used in which the eyes were frozen by merely placing them in the container immersed



Fig 6—Opaque corneal graft, showing absorption along the borders and replacement with scar tissue. Donor material had been frozen in liquid nitrogen

in the liquid nitrogen. Another series was prepared in which the eyes were first placed in a previously cooled small flask containing isopentane which caused the eyes to freeze more rapidly. This flask was then immersed in the liquid nitrogen. After freezing, the eyes were placed in a refrigerator compartment which kept the temperature at  $-40^{\circ}\text{C}$ .

When ready for use, the eyes were removed from the refrigerator, and approximately two hours was required for "thawing out." At the end of this time the cornea had returned to nearly normal transparency, but it had lost some of its normally firm consistency. This was true whether the eye was frozen directly in liquid nitrogen or immersed in the isopentane solution. Both gave the same results. When this material was used for corneal transplantation, the graft retained a reasonable amount of transparency for about one week but thereafter gradually became opaque (fig 6). As illustrated in figure 6, the graft showed some absorption and replacement of the donor material with scar tissue. The opacity was dense, and microscopic section (fig 7) revealed almost complete fibrosis of the graft.

## CONCLUSIONS

From the preceding data, it is apparent that corneal tissue will remain clear and of normal thickness and can be used suitably for transplantation up to a period of three days. Thereafter the tissue becomes progressively hazy and thickened, being thus rendered unsuitable for grafting. After three days there may be areas of transplanted cornea that tend to retain transparency, but tissue kept for one week becomes uniformly opaque. For keeping corneal tissue clear, a solution may be used that is as nearly isotonic with the body fluids as possible—whether this be saline solution, Hartmann's solution or blood plasma. It is evident, however, that the tissue in question will not survive for long periods outside the body and retain its normal characteristics.

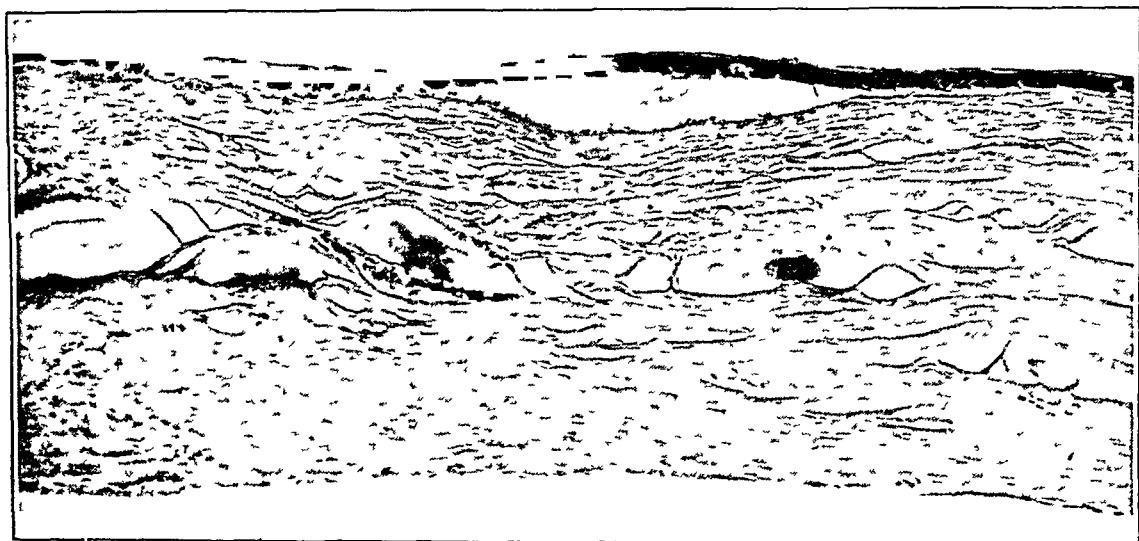


Fig 7—Microscopic section of the corneal graft seen in figure 6. There are infiltration, disorganization of the stromal layers and fibrosis.

After frozen corneal tissue returned to normal body temperatures, it regained its original transparency, but here, again, there had been some loss in the viability of the tissue, as it invariably became opaque with transplantation.

It can be concluded from this study that corneal tissue to be used for transplantation should be obtained from a fresh specimen and used within a relatively short period in order to obtain the best surgical results. In general it has been observed that these experimental data can be applied to clinical cases, and the general principles here set forth should be followed in the preservation of human tissue for corneal transplantation.

# Ophthalmologic Reviews

EDITED BY DR FRANCIS HEED ADLER

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## METABOLISM OF THE RETINA

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AND

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**D**URING the past few years the interest in retinal metabolism has been greatly intensified. Many investigations were made on the retina as part of a war emergency program. Because of this practical interest in a narrow but important subdivision of ophthalmology, this survey of the literature was made.

A study of the metabolic processes in the retina has been the basis of much research, particularly within the last ten years. This is not surprising, as such work may have a double goal—first, to provide additional information on the problem of visual mechanisms and, second, inasmuch as the retina shows metabolic activity greater than that of almost any other tissue, to study the chain reactions of intermediate metabolism. The extensive literature, dealing with many phases of the problem, is difficult to put together into a single picture, and therefore one must present many observations alone and await further investigation to understand fully their significance. In this paper no attempt is made to discuss the mechanism of the visual pigments, although their reactions are certainly a part of retinal metabolism. The discussion is limited chiefly to carbohydrate metabolism, with reference to a possible fat and protein metabolism. It is to be remembered that the process observed in a complex organ such as the retina may represent the summation of metabolic processes connected with the visual mechanism, the transmission of impulses along nerve fibers and across the synapses and the basal metabolism of the cells involved.

### METHODS AND MATERIAL

These studies were made on retinas obtained from the eyes of various animals, principally the frog, rat, rabbit and ox. In many cases unexplained species variation may add to the difficulty in comparing results. Studies of oxygen utilization, carbon dioxide production, aerobic and anaerobic glycolysis and ammonia produc-

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tion were made with the Warburg manometer, employing the entire retina, sliced or minced retinas, retinal extracts or, occasionally, special slices including only certain regions or layers of the retina. The effect of various added substrates or poisons, as well as the production of final or intermediate products, was determined with this method. The Thunberg method was employed for determination of dehydrogenases. Measurements of the  $p_H$  were usually made with the hydrogen electrode. Acetylcholine was determined by bioassay, using the magnitude of muscular contraction as compared with a standard. The effects of light and dark adaptation were found by illuminating one eye of an animal, the lids being held open and the eye irrigated, while the other eye was blindfolded to serve as the control, and then quickly placing the retinas in the manometer vessels. The effect of illuminating and darkening the vessels was also investigated.

Determinations on the human retina were limited to a few cases in which the eye was enucleated, usually for glaucoma or tumor, and to the indirect observations in which the effect of anoxia and carbon dioxide excess on the dark adaptation and the visual acuity of volunteer subjects was noted.

## RESULTS

*Hydrogen Ion Concentration*—The early work of Chodín<sup>1</sup> in 1878, and of Kuhne<sup>2</sup> and Cahn,<sup>3</sup> shortly thereafter, showed little change in the slightly alkaline retina on exposure to light, yet Angelucci,<sup>4</sup> at about the same time, first demonstrated the shift toward the acid side on illumination, which fact has subsequently been often confirmed. Lodato,<sup>5</sup> in 1900, stated that the greatest acidification was given by light of short wavelength and also demonstrated how thermal, electrical or chemical irritation could produce acidity. Majima,<sup>6</sup> however, showed that yellow and green light were more effective. Re<sup>7</sup> produced acidity by stimulation of the optic tract. Quantitative studies by Nakashima<sup>8</sup>

1 Chodín, A. Ueber die chemische Reaktion der Netzhaut und des Sehnerven, Sitzungsber d k Akad d Wissensch Math-naturw Cl **76** 121, 1878.

2 Kuhne, W. Chemische Vorgänge in der Netzhaut, in Hermann, L. Handbuch der Physiologie, Leipzig, F. C. W. Vogel, 1879, vol. 3, p. 234.

3 Cahn, A. Zur physiologischen und pathologischen Chemie des Auges, Ztschr f physiol Chem **5** 213, 1881.

4 Angelucci, A. Histologische Untersuchungen über das retinale Pigmentepithel der Wirbelthiere, Arch f Physiol, 1878, p. 353.

5 Lodato, G. Immutamenti della retina sotto l'influenza della luce, dei colori e di altri agenti fisici e chimici, con speciale riguardo alla reazione chimica contributo alla fisiologia della retina, Arch di ottal **7** 335, 1900, abstracted, Klin Monatsbl f Augenh **38** 365, 1900.

6 Majima, K. Studien über die Struktur der Sehzellen und der Pigmentepithelzellen der Froschnetzhaut, Arch f Ophth **115** 286, 1925.

7 Re, F. Sulle modificazioni fisiche e chimiche della retina per l'eccitazione elettrica dell'encefalo, mesencefalo e chiasma, Arch di ottal **12** 147, 1904, abstracted, Arch d'ophth **26** 123, 1906.

8 Nakashima, M. Beiträge zur Kenntnis des Sehpurpurs XIII Internationaler Ophthalmologenkongress, Amsterdam, 1929, abstracted, Zentralbl f d ges Ophth **22** 772, 1930.

showed the  $p_H$  of the dark-adapted retina to be about 7.3 and that of the light-adapted retina to be about 7.0

That this change may be related to the activity of the visual cells rather than of the nerve elements and may vary with the type of cell was shown in 1937 by von Studnitz,<sup>9</sup> who found no change in the  $p_H$  of the guinea pig retina, which contains only rods, while the cat and fish retinas, which contain also cones, showed a shift to the acid side. The acidity increased with time, corresponding to the regeneration of visual substances. The production of acid increased with elevation in temperature, as well as with greater intensity of light. After fifteen minutes of illumination acidification decreased (probably through the exhaustion of visual substance reserves) but rose again after twenty to twenty-five minutes (probably because of supplementary visual substances). The curve of acid production at different wavelengths of light for the reptile corresponds to the absorption curve of the cone substance, being greatest with yellow light. Von Studnitz' further work<sup>10</sup> showed little change in  $p_H$  on illuminating the retinas of selachians and cephalopods, which contain only rods. He expressed the belief that acidification of the retina leads to contraction of the cones and expansion of pigment. Dittler,<sup>11</sup> in 1907, showed that an aqueous extract of a light-adapted retina caused the contraction of cones in a dark-adapted retina, similar to the stimulation of light.

*Organic Phosphate*—A study of the phosphoric acid and phosphoric esters in the retina, particularly because of their importance in intermediate carbohydrate metabolism, may provide important information concerning the sources of energy for visual processes. Lange and Simon,<sup>12</sup> in 1922, showed that frog retina contains 0.08 per cent phosphoric acid. A phosphate ester apparently present in the outer segments of the rods of the frog and carp was hydrolyzed in alkaline solution into phosphoric acid and an organic substance. An increase of phosphoric acid in the vitreous of a removed eye was noted on high illumination, a partial reformation of the phosphate ester took place only if the retina was removed with the pigment epithelium, yet no phosphate was obtained from the pigment epithelium alone on illumination. The organic phosphate compound was not hexose phosphate, but probably

9 von Studnitz, G. Die retinale Säurebildung, Arch f d ges Physiol **238** 802, 1937

10 von Studnitz, G. Ueber die chemische Reaktion der Selachier- und Cephalopodenretina, Ztschr f vergl Physiol **19** 615, 1933

11 Dittler, R. Ueber die chemische Reaktion der isolierten Froschnetzhaut, Arch f d ges Physiol **120** 44, 1907

12 Lange, H., and Simon, M. Ueber Phosphorsäureausscheidung der Netzhaut bei Belichtung, Ztschr f physiol Chem **120** 1, 1922

phosphocreatine Tawara<sup>13</sup> found two types of organic phosphate in the retina which liberated inorganic phosphate on illumination, one of which appeared to be phosphocreatine, the other a soluble phosphate ester Kuzuya,<sup>14</sup> also working with the rabbit retina, demonstrated an acid-soluble and an acid-insoluble phosphate compound He also investigated the changes in the amount of these different phosphate fractions with the growth of the rabbit<sup>15</sup>

Nakashima and Arata<sup>16</sup> considered the possibility that phosphoric acid arose from the splitting of phosphocreatine in a manner analogous to that occurring in muscle but presented evidence against the photolysis of phosphocreatine They showed that it is the Kjeldahl nitrogen (choline, carnosine) which increases on illumination and proposed the theory that phosphoric acid arises through the photolysis of retinal lipids They stated the belief that phosphocreatine nitrogen, which increased with damage to the tissue and was inhibited by light, occurred through the autolysis of the retina

Takamatsu<sup>17</sup> demonstrated that the isolated retinas of frogs and white rats produced phosphoric acid in Ringer's solution (isotonic solution of three chlorides U S P ) even in the dark, probably as the result of autolysis Within limits, the increased production of phosphoric acid on illumination varied with length of exposure That this process was reversible was shown by the fact that on darkening the once lighted retina production of phosphoric acid could again be demonstrated on illumination Illumination of the retina of the white rat produced a reduction of phosphatide content He further showed<sup>18</sup> that in frogs and rabbits poisons which produced acute amaurosis or amblyopia, such as methyl alcohol and quinine, decreased the phosphate ester content

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13 Tawara, M The Effect of Light upon the Phosphoric Acid Fraction of the Retina, *Acta Soc ophth jap* **42**:1503, 1938, abstracted, p 106

14 Kuzuya, N Veränderung des Gehalts von verschiedenen Phosphorsäurefraktionen in Hell- und Dunkelnethzhaut, *Acta Soc ophth jap* **41**:637, 1937; abstracted, p 51

15 Kuzuya, N Veränderung des Gehaltes der Netzhaut an verschiedenen Phosphorsäurefraktionen mit dem Wachstum, *Acta Soc ophth jap* **41** 335, 1937; abstracted, p 28

16 Nakashima, M, and Arata, Y Azotometria der Netzhaut, *Acta Soc ophth jap* **40** 1586, 1936, abstracted, p 97

17 Takamatsu, T Photochemische Studien der Netzhaut II Ueber die Phosphorsäurebildung und die Phosphatidveränderung der Netzhaut bei Lichtung, *Acta Soc ophth jap* **38** 1035, 1934, abstracted, p 71

18 Takamatsu, T Photochemische Studien der Netzhaut III Ueber den Einfluss der Gifte (Methylalkohol, Chinin) auf die Phosphorsäurebildung der Netzhaut bei Belichtung, *Acta Soc ophth jap* **39** 598, 1935, abstracted, p 54



Von Studnitz<sup>19</sup> assumed that light decomposed the cone substance, with the production of phosphoric acid, expansion of pigment and contraction of cones, and as proof he showed that the injection of this acid into the dark-adapted retina produced a configuration of the cones and pigment for light, while injection of alkali into light-adapted retinas resulted in a configuration for the dark. There was a parallel change in the light absorption curves with injection of acid and of alkali. He expressed the belief that the cones alone show motility.

The increase in electrical conductivity of a solution of visual purple in the light and the decrease in the dark, as measured by Lasareff,<sup>20</sup> was probably due to the reversible hydrolysis of organic phosphate.

Evidence would indicate, however, that the acid reaction on illumination previously mentioned is probably due to the production of lactic acid in glycolysis rather than to the aforementioned liberation of phosphoric acid.

*Oxidation-Reduction Potential*—Nakashima<sup>21</sup> found that the oxidation-reduction potential of suspensions of frog retinas increased on illumination and decreased in the dark, while he and Hayashi<sup>22</sup> showed that at the same time the consumption of oxygen was unchanged. Iron, enzymes and lipid apparently took part in the transfer of electrons, as the potential was decreased by potassium cyanide and the prolonged action of toluene and was increased by iron salts. The change did not depend on the presence of visual purple.

*Respiration and Glycolysis*—The unique respiratory activity of the retina has led to its extensive study. Warburg,<sup>23</sup> in 1927, showed that the retina had the highest rate of respiration and of anaerobic glycolysis of any tissue studied and an extremely high anaerobic glycolysis, which even surpassed that of most tumors. Kubowitz,<sup>24</sup> Negelein<sup>25</sup> and

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19 von Studnitz, G. Vom Energieumsatz in der Netzhaut, *Naturwissenschaften* **22** 193, 1934.

20 Lasareff, P. Sur le changement de la conductibilité électrique du pourpre visuel au cours de l'éclairage, *Compt rend Acad d sc* **181** 476, 1925.

21 Nakashima, M. Ueber das Oxydations-Reduktions-Potential der Netzhaut, *Ber u d Versamml d deutsch ophth Gesellsch* **47** 369, 1929.

22 Nakashima, M., and Hayashi, K. Sur le potentiel d'oxydo-reduction de la rétine, *J Biochem* **17** 315, 1933.

23 Warburg, O. Ueber die Klassifizierung tierischer Gewebe nach ihrem Stoffwechsel, *Biochem Ztschr* **184** 484, 1927.

24 Kubowitz, F. Stoffwechsel der Froschnetzhaut bei verschiedenen Temperaturen und Bemerkung über den Meyerhofquotienten bei verschiedenen Temperaturen, *Biochem Ztschr* **204** 475, 1929.

25 Negelein, E. Ueber die glykolytische Wirkung embryonalen Gewebes, *Biochem Ztschr* **165** 122, 1925.

Oguchi,<sup>26</sup> working with frogs, and Nakashima,<sup>27</sup> using fish, demonstrated that in these cold-blooded animals the anaerobic glycolysis increased with the temperature and was much greater than the aerobic glycolysis up to 37 C, after which the aerobic glycolysis predominated. This effect of temperature was confirmed for mammalian and avian retinas by Warburg and associates,<sup>28</sup> Krebs<sup>29</sup> and Schmitz-Moormann.<sup>30</sup> Oguchi<sup>31</sup> compared the rates of respiration and glycolysis in birds, fish and frogs and found values for both to be highest in birds and least in frogs. Warburg and associates<sup>28</sup> suggested that the lactic acid produced aerobically from glucose was the result of trauma to the retina. In studying the lactic acid production of the retina of growing chickens, Tamiya<sup>32</sup> obtained the highest values during the period of growth and a decrease on maturity.

There appears to be a distinct difference between warm-blooded and cold-blooded animals in the effect of light on respiration and glycolysis. Kiyohara<sup>33</sup> reported that the dark-adapted retina of the toad took up 3.9 cu mm of oxygen per milligram hour, while the light-adapted retina took up 2.8 cu mm. Jongbloed and Noyons<sup>34</sup> showed the oxygen consumption to be 26.5 per cent higher and the carbon dioxide production 25 per cent higher in dark-adapted than in light-adapted retinas of the frog. Similar results were obtained in the frog by Noyons and Wier-

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26 Oguchi, T. Ueber den Stoffwechsel der Netzhaut. II. Der Stoffwechsel der Netzhaut der Reptilien, der Stoffwechsel der Netzhaut nach dem Tode des Froschen, *Acta Soc ophth jap* **36** 1702, 1932.

27 Nakashima, M. Stoffwechsel der Fischnetzhaut bei verschiedenen Temperaturen, *Biochem Ztschr* **204** 479, 1929.

28 Warburg, O., Posener, K., and Negelein, E. Ueber den Stoffwechsel der Carcinomzelle, *Biochem Ztschr* **152** 308, 1924.

29 Krebs, H. A. Ueber den Stoffwechsel der Netzhaut, *Biochem Ztschr* **189** 57, 1927.

30 Schmitz-Moormann, P. Ueber den Glykogengehalt der Retina und seine Beziehungen zur Zapfenkontraktion, *Klin Monatsbl f Augenh* **78** 69, 1927.

31 Oguchi, T. Ueber den Stoffwechsel der Netzhaut. I. Der physiologische Stoffwechsel der Netzhaut der verschiedenen Tierarten, der Stoffwechsel der Netzhaut nach dem Tode der Tiere, *Acta Soc ophth jap* **36** 1203, 1932.

32 Tamiya, C. Ueber den Stoffwechsel der Netzhaut in verschiedenen Stadien ihrer Entwicklung, *Biochem Ztschr* **189** 114, 1927.

33 Kiyohara, K. Ueber die Wirkung der Strahlen verschiedener Wellenlangen auf die Sauerstoffatmung der Netzhaut, *Nagasaki Igakkai Zasshi* **9** 730, 1931, abstracted, p 735.

34 Jongbloed, J., and Noyons, A. K. M. Sauerstoffverbrauch und Kohlendioxydproduktion der Froschretina bei Dunkelheit und bei Licht, *Ztschr f Biol* **97** 399, 1936.

sma<sup>35</sup> and Lindeman<sup>36</sup> Ikemune<sup>37</sup> found a 10 per cent greater carbon dioxide production from the frog retina in the dark than on illumination and noted that the production was greater for longer periods of dark adaptation. He<sup>38</sup> reported that the glucose concentration of light-adapted retinas averaged 91 mg per hundred cubic centimeters, while for dark-adapted retinas it averaged 20 to 79 mg per hundred cubic centimeters. He interpreted these results as showing that the resynthesis of visual purple in the dark occurred with the energy of glucose metabolism and that the increase in carbon dioxide production was related to the increase in glycolysis.

On the other hand, Galante<sup>39</sup> found that light increased the oxygen consumption of the dove and sparrow retina, and Takano<sup>40</sup> demonstrated that in the rat the rate of respiration, as well as the aerobic glycolysis, increased on illumination of the dark-adapted retina. He<sup>41</sup> found that small differences in the duration, intensity or color of the light had no effect on the change. Yet, also working with the rat, Campos<sup>42</sup> obtained higher oxygen consumption in the dark-adapted than in the light-adapted retina. Kodama<sup>43</sup> compared the respiratory rate in vessels in the light and in the dark, perhaps a different matter than comparing the respiratory activity of light-adapted and of dark-adapted eyes, and found that the oxygen consumption and aerobic glycolysis were much greater in the dark than in the light for the first thirty minutes but then fell, approaching that of the retina in the light.

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35 Noyons, A. K. M., and Wiersma, C. A. G. L'influence de la lumiere sur la consommation d'oxygene de la retine de l'œil de grenouille, *Acta brev. Neerland.* **3** 156, 1933.

36 Lindeman, V. F. The Respiratory Metabolism of the Frog Retina, *Physiol. Zool.* **13** 411, 1940.

37 Ikemune, I. Einfluss des Lichtes auf die CO<sub>2</sub>-Produktion der Netzhaut, *Okayama-Igakkaï-Zasshi* **51** 529, 1939, abstracted, p. 538.

38 Ikemune, I. Der Einfluss des Lichtes auf die Glykolyse in der Froschnetzhaut, *Okayama-Igakkaï-Zasshi* **51** 539, 1939, abstracted, p. 543, Der Einfluss des Lichtes auf die Glykolyse in der Froschnetzhaut, *Jap. J. M. Sc.* **III**, Biophysics **5** 90, 1938.

39 Galante, E. L'azione dell'eccitamento retinico sul ricambio gassoso, *Ann. di clin. med.* **20** 79, 1930.

40 Takano, M. Ueber die Gewebsatmung der Netzhaut der Ratte, *Acta Soc. ophth. jap.* **38** 1307, 1934, abstracted, p. 85.

41 Takano, M. Ueber die Gewebsatmung der Netzhaut der Ratte. II. Ueber die Einflüsse der kurzen Beleuchtung des farblosen Lichtes und der dauernden Beleuchtung des farbigen Lichtes auf die Gewebsatmung und aerobe Glykolyse der Netzhaut, *Acta Soc. ophth. jap.* **39** 162, 1935, abstracted, p. 17.

42 Campos, R. Ricerche sul ricambio della retina, *Ann. di ottal. e clin. ocul.* **64** 456, 538 and 577, 1936.

43 Kodama, S. Studien über den Gaswechsel der Netzhaut der Ratte, *Tohoku J. Exper. Med.* **28** 423, 1936.

The oxygen consumption was not proportional to the intensity of the light. In colored light the oxygen consumption and aerobic glycolysis were greatest in red, less in green and least in blue light. In the dark, in dextrose-free Ringer's solution the oxygen consumption was high but fell rapidly to zero. In 0.1 per cent dextrose the oxygen consumption was high at first but fell rapidly to a fifth of its original value, and the aerobic glycolysis was high and decreased but little. In 0.4 per cent dextrose the oxygen consumption and aerobic glycolysis were comparatively low at the start and decreased only slightly. The anaerobic glycolysis was equally high in Ringer's solution containing 0.1, 0.2 and 0.4 per cent dextrose.

Working with the peripheral and central parts of monkey eyes, Campos<sup>44</sup> showed that both parts of the lighted retina showed less oxygen consumption than the dark-adapted retina, the values rising during the experiment and approaching the value for the dark-adapted retina. Glycolysis of the macula of the illuminated eye was less than that of the dark-adapted eye, while the peripheral parts showed no difference on illumination. Campos<sup>42</sup> measured the exchange of gases in human eyes removed six to ten days after injury and development of glaucoma. There was a high rate of respiration and of aerobic and anaerobic glycolysis, particularly the former. There was no excess of glycolysis, and the Pasteur effect was low or absent. The peripheral retina showed more active respiration than the macula except in cases of absolute glaucoma. He also examined the retinas of albino rats and found slightly more active respiration but definitely lower aerobic glycolysis than in pigmented retinas.

*Anoxia*—Santoni<sup>45</sup> noted the effect of interrupting retinal circulation by ligating the entire orbital contents of rabbits and rats for fifteen to ninety minutes. He found that the oxidizing power increased after interruption for fifteen to thirty minutes but decreased after sixty to ninety minutes. De Crecchio<sup>46</sup> produced anoxia by compressing the globe of rabbits for thirty to one hundred and eighty minutes; anaerobic glycolysis was decreased after sixty minutes but increased after ninety or one hundred and eighty minutes. They expressed the belief that the decrease in glycolysis and the increased respiratory rate indicated degenerative changes as a result of ischemia, with the freeing of substances such as fats.

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44 Campos, R. L'azione della luce sulla respirazione e sulla glicolisi della retina, *Boll. Soc. ital. di biol. sper.* **11** 320, 1936.

45 Santoni, A. Il ricambio della retina dopo interruzione della circolazione retinica, *Ann. di ottal. e clin. ocul.* **67** 299, 1939.

46 de Crecchio, A. Il ricambio della retina dopo compressione del bulbo, *Ann. di ottal. e clin. ocul.* **67** 739, 1939, abstracted, *Arch. Ophth.* **24** 1016 (Nov.) 1940.

The effect of anoxia in the human retina has been studied by many investigators. McFarland and Evans,<sup>47</sup> Gellhorn,<sup>48</sup> McDonald and Adler<sup>49</sup> and McFarland and Halperin<sup>50</sup> proved that lack of oxygen, excess of carbon dioxide or hyperpnea decreased visual acuity and dark adaptation. McFarland and Forbes<sup>51</sup> showed a similar effect of hypoglycemia. Vitamin A deficiency did not alter the effect of lack of oxygen. It undoubtedly acts by a different mechanism. It is probable that these changes were not concerned with the photochemical substances but involved the neural elements of the retina. In relation to avitaminosis A, however, de Leonibus<sup>52</sup> found that in albino rats placed on a deficiency diet until keratomalacia developed there was no change in oxygen consumption but that glycolysis was 86 per cent higher in the avitaminotic animals.

With atrophy of the retina produced experimentally by cutting the optic nerve in cats, Adler<sup>53</sup> showed there was an increased concentration of sugar in the vitreous. The glycolytic activity of the atrophied retinas, however, was decreased. In this manner the hypothesis that the low concentration of sugar in the vitreous is due to the high rate of glycolysis in the normal retina was confirmed. Craig and Beecher<sup>54</sup> observed that twice as much lactic acid was produced by the rat retina in phosphate as in bicarbonate buffer. In phosphate buffer there was a 38 per cent lower rate of respiration in 10 per cent oxygen and a 51 per cent lower respiratory rate in 5 per cent oxygen than in 100 per cent oxygen. The rates of respiration and glycolysis showed a reciprocal relationship to each other as the oxygen tension varied. In bicar-

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47 McFarland, R. A., and Evans, J. N. Alterations in Dark Adaptation Under Reduced Oxygen Tensions, *Am J Physiol* **127** 37, 1939.

48 Gellhorn, E. The Effect of O<sub>2</sub> Lack, Variations in the CO<sub>2</sub>-Content of the Inspired Air, and Hyperpnea on Visual Intensity Discrimination, *Am J Physiol* **115** 679, 1936.

49 McDonald, R., and Adler, F. H. Effect of Anoxemia on the Dark Adaptation of the Normal and of the Vitamin A-Deficient Subject, *Arch Ophth* **22** 980 (Dec.) 1939.

50 McFarland, R. A., and Halperin, M. H. The Relation Between Foveal Visual Acuity and Illumination Under Reduced Oxygen Tension, *J Gen Physiol* **23** 613, 1940.

51 McFarland, R. A., and Forbes, W. H. Effects of Variation in the Concentration of Oxygen and of Glucose on Dark Adaptation, *J Gen Physiol* **24** 69, 1940.

52 de Leonibus, F. Il ricambio della retina in avitaminosi A, *Ann di ottal e clin. ocul* **67** 512, 1939.

53 Adler, F. H. The Metabolism of the Retina. Further Notes, *Arch Ophth* **6** 901 (Dec.) 1931.

54 Craig, F. N., and Beecher, H. K. The Effect of Low Oxygen Tension on Tissue Metabolism (Retina), *J Gen Physiol* **26** 467, 1943.

bonate buffer, on the other hand, there was no sign of change in respiration with the oxygen tension lowered from 95 to 5 per cent, but glycolysis was increased nearly to anaerobic levels. Dickens and Greville<sup>55</sup> found that the rat retina, as well as the brain, oxidizes fructose strongly, although their earlier work<sup>56</sup> would indicate that in the case of the retina there is not an intermediate conversion into lactic acid, as they noticed negligible production of lactic acid from fructose. Chase and Hagan<sup>57</sup> proved that lack of oxygen does not alter the changes in the absorption spectrum of visual purple, thus giving further evidence that lack of oxygen affects only the neural elements of the retina.

*General Metabolism*—Much information about normal retinal metabolism, as well as facts concerning pathologic conditions, has been gained by studying the effect of various poisons on metabolic changes. Holmes<sup>58</sup> and Lenti<sup>59</sup> showed that fluoride inhibited lactic acid formation from glucose, prevented the disappearance of inorganic phosphate and allowed no accumulation of phosphate esters, thus indicating that fluoride inhibits the first stage of glucose breakdown. Dickens and Greville<sup>56b</sup> noted that the inhibition of anaerobic glycolysis in a tissue parallels the magnitude of the glycolysis, and thus retina, with the highest glycolytic activity, was inhibited by less than 1 millimol of fluoride. Kerly and Bourne<sup>60</sup> found that in fluoride-poisoned extracts there was some formation of an ester which was hydrolyzed with difficulty from glucose and that its formation was increased by addition of pyruvic acid.

Lenti<sup>59</sup> also showed that a two-hundredth molar solution of iodoacetate inhibited glycolysis but that phlorhizin did not. On the contrary, de

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55 Dickens, F, and Greville, G D. The Metabolism of Normal and Tumour Tissue. III. Respiration in Fructose and in Sugar-Free Media, *Biochem J* **27** 832, 1933.

56 Dickens, F, and Greville, G D. (a) The Metabolism of Normal and Tumour Tissue. VI. The Conversion of Fructose and Glucose to Lactic Acid by Embryonic Tissue, *Biochem J* **26** 1251, 1932, (b) VII. The Anaerobic Conversion of Fructose into Lactic Acid by Tumour and Adult Normal Tissues, *ibid* **26** 1546, 1932.

57 Chase, A M, and Hagan, W H. The Photochemical and Thermal Reactions of Visual Purple in Absence of Oxygen, *J Cell & Comp Physiol* **21** 65, 1943.

58 Holmes, B E. Inhibition by Fluoride of Glucose Breakdown in Tumour Tissue and Retina Extracts, *Biochem J* **34** 926, 1940.

59 Lenti, C. Glycolysis in the Retina, *Arch dis c Biol* **25** 455, 1939, abstracted, *Chem Abstr* **34** 5903, 1940.

60 Kerly, M, and Bourne, M C. Glycolysis in Retinal Extracts, *Biochem J* **34** 563, 1940.

Concilus <sup>61</sup> found that 0.02 to 0.01 millimol of phlorhizin had a strong inhibiting action on glycolysis, proportional to the concentration, there was little effect on the respiration, the action apparently being specific for glycolysis. Bisulfite and hydrazine inhibited glycolysis without the formation of methylglyoxal, triose or pyruvic acid. Sullmann and Vos <sup>62</sup> found phosphorylation and lactic acid formation are inhibited by glyceraldehyde and one-fortieth molar maleic acid. Kerly and Bourne <sup>60</sup> and Lenti <sup>59</sup> also observed the inhibitory effect on glycolysis of glyceraldehyde. Greville <sup>63</sup> noticed that in tissue with pure carbohydrate respiration, such as the retina, the respiration was inhibited by malonate but fumarate only partially relieved the inhibition.

Oguchi <sup>64</sup> showed that poisons, such as methyl alcohol, quinine and illuminating gas, which injure vision, also reduce the oxygen consumption 25 to 50 per cent in vitro. Wolff <sup>65</sup> reported that quinine if injected into the vitreous, and thus brought in direct contact with the retina, rapidly inhibited respiration but that subcutaneous injections did not inhibit oxygen consumption, even though complete amaurosis occurred. Only after repeated doses was any effect noted. Califaro <sup>66</sup> demonstrated how retinal glycolysis was inhibited by the agents which inhibit muscular glycolysis. Oguchi <sup>67</sup> showed that, while after the injection of 0.1 mg. of thyroxin per hundred grams of body weight the respiratory activity of the retina increased, the injection of one-tenth this amount produced a fall in the respiratory rate up to 20 per cent and a fall in glycolysis up to 30 per cent.

For the rat retina Laser <sup>68</sup> showed that carbon monoxide did not inhibit the oxygen uptake even in high concentration, however, it inhibits the Pasteur effect, aerobic equaling anaerobic glycolysis.

61 de Conciliis, N. Ricerche sulla fosfatasi retinica, Sperimentale, Arch di biol **88** 793, 1934

62 Sullmann, H., and Vos, T. A. Der glykolytische Kohlenhydrataufbau in Extrakten der Retina, Enzymologia **6** 246, 1939

63 Greville, G. D. Fumarate and Tissue Respiration. I. The Effect of Dicarboxylic Acids on the Oxygen Consumption, Biochem J **30** 877, 1936

64 Oguchi, T. Ueber den Stoffwechsel der Netzhaut. IV. Ueber den Einfluss der Gifte (Methylalcohol, Chinin und Leuchtgas) auf den Stoffwechsel der Netzhaut, Acta Soc ophth jap **36** 1997, 1932, abstracted, p 155

65 Wolff, E. The Effect of Quinine on the Oxygen Consumption of the Dog's Retina, Tr Ophth Soc U Kingdom **56** 162, 1936

66 Califaro, L. Ricerche sulla glicolisi della retina, Atti d Accad Lincei **25** 93, 1937

67 Oguchi, T. Ueber den Stoffwechsel der Netzhaut. V. Ueber den Einfluss des Thyroxins auf den Stoffwechsel der Netzhaut, Acta Soc ophth jap **37** 103, 1933, abstracted, p 6, VI. Weiteres über den Einfluss des Thyroxins auf den Stoffwechsel der Netzhaut, ibid **37** 956, 1933, abstracted, p 72

68 Laser, H. Tissue Metabolism Under the Influence of Carbon Monoxide, Biochem J **31** 1677, 1937

Elliott and Baker<sup>69</sup> found that the oxidation-reduction potential indicator 2,6-dichlorophenolindophenol in  $1.3 \times 10^{-3}$  concentration produced almost complete inhibition of respiration in the presence or absence of dextrose. According to Oyama,<sup>70</sup> the optimum  $p_H$  for respiration was 8.0 to 8.5. He also showed that the oxygen consumption of the temporal and that of the nasal half of the retina were the same. Between  $p_H$  6.88 and 7.88 he found that the oxygen consumption increased with increasing alkalinity.<sup>71</sup>

The respiratory rate of rat retina was about twice as high in bicarbonate Ringer's solution as in phosphate Ringer's solution. Laser<sup>72</sup> also found that hydrocyanic acid inhibited the respiration of the retina in phosphate Ringer's but not in bicarbonate Ringer's solution. Craig and Beecher<sup>73</sup> observed that the metabolism of rat retina was sensitive to the concentration of the carbon dioxide-bicarbonate buffer system. Increasing the carbon dioxide concentration from 1 to 5 per cent at constant  $p_H$  almost doubled both the oxygen consumption and the glycolysis, increasing it from 5 to 20 per cent had no effect on glycolysis but depressed the oxygen uptake from 31 to 19. In mediums containing dextrose and 1 per cent carbon dioxide-bicarbonate buffer the addition of succinate increased the oxygen uptake from 12 to 16 without affecting glycolysis, succinate, however, had no effect on a medium containing dextrose and phosphate.

Shaffer, Chang and Gerard,<sup>74</sup> in studying the influence of blood constituents on tissue metabolism, reported that in dog retina the oxygen consumption was 187 per cent greater in serum than in Ringer's solution, in other tissues this increase is related to serum proteins. Ideta<sup>75</sup> observed the effect of sugar concentration on the metabolism of rabbit retina and found that the respiratory rate increased

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69 Elliott, K. A. C., and Baker, Z. The Effects of Oxidation-Reduction Potential Indicator Dyes on the Metabolism of Tumour and Normal Tissues, *Biochem J* **29** 2396, 1935.

70 Oyama, N. Einfluss der Wasserstoffionenkonzentration auf den Sauerstoffverbrauch der Hellnetzhaut von Kaninchen in vitro, *Tohoku J Exper Med* **35** 576, 1939.

71 Oyama, N. Einfluss des Natriumbikarbonats auf den Sauerstoffverbrauch der Hellnetzhaut von Kaninchen in vitro, *Tohoku J Exper Med* **37** 78, 1939, abstracted, *Chem Abstr* **34** 2051, 1940.

72 Laser, H. Metabolism of Retina, *Nature, London* **136** 184, 1935.

73 Craig, F. N., and Beecher, H. K. The Effect of Carbon Dioxide Tension on Tissue Metabolism (Retina), *J Gen Physiol* **26** 473, 1943.

74 Shaffer, M., Chang, T. H., and Gerard, R. W. The Influence of Blood Constituents on Oxygen Consumption in Nerve, *Am J Physiol* **111** 697, 1935.

75 Ideta, K. Studien über die Gewebsatmung der Netzhaut des Kaninchens in Vitro. Einfluss des Zuckers im Serum, *Jap J M Sc, III, Biophysics* **5** 105, 1938.



with increasing sugar concentrations up to a maximum at 0.5 per cent, while glycolysis was greatest at a concentration of 0.2 to 0.4 per cent. Oguchi<sup>76</sup> also noted that the metabolism of rabbit retina was greater in serum than in Ringer's solution. Aerobic glycolysis was present in serum, but the Pasteur effect was prominent. In both mediums the temperature coefficient increased slowly with time, this increase, the author stated, indicating tissue damage.

Considerable information on the chemical changes which take place in retinal metabolism has been gained in recent years by groups of investigators who have studied the formation and effect of intermediary products. In 1935 Possenti<sup>77</sup> observed that the aerobic and anaerobic glycolysis of the retina was higher than that of any other normal tissue and was comparable to that of tumor tissue. The production of lactic acid from dextrose was higher than that from hexosediphosphoric acid. From  $\alpha$ -glycerophosphoric acid and phosphoglyceric acid, although they were actively metabolized, the lactic acid production was very small and was not influenced by mixing  $\alpha$ -glycerophosphoric acid and phosphoglyceric acid or by the addition of pyruvic acid to  $\alpha$ -glycerophosphoric acid. Hexosediphosphoric acid,  $\alpha$ -glycerophosphoric acid and phosphoglyceric acid showed an induction period for formation of lactic acid, probably due to dephosphorylation. They found no liberation of phosphoric acid from the retina during glycolysis.

Sullmann and Vos<sup>62</sup> asserted that an extract of ox retinas inactivated by dialysis was able to produce lactic acid after the addition of muscle adenylic acid. Cozymase alone could not activate it. Manganese, magnesium and pyruvic acid increased the formation of lactic acid. While dextrose, mannose and fructose were equivalent as substrates, galactose yielded only small amounts of acid. Hexosediphosphate gave much less lactic acid than did dextrose, but dextrose-1-phosphate gave as much. Inorganic phosphate was found necessary for glycolysis. Nicotinic acid, nicotine or nicotinamide had no stimulatory effect on metabolism. When inosinic acid was used instead of adenylic acid, there was no phosphorylation or lactic acid production. In a subsequent study Sullmann<sup>78</sup> found that inosinic acid could function in retinal extracts as a coenzyme in the phosphorylation of both glucose and glycogen, although not as effectively as adenylic acid.

76 Oguchi, T. Experimentelle Studien über den Einfluss des verschiedenartigen Bedingungen auf den Stoffwechsel der Netzhaut. I. Der physiologische Stoffwechsel der Kaninchennetzhaut in Ringerlösung und im Serum, *Acta Soc ophth jap* **40** 1568, 1936, abstracted, p. 96.

77 Possenti, G. Prime ricerche sulla glicolisi retinica, *Riv di pat sper* **15** 183, 1935.

78 Sullmann, H. Ueber die CO-Enzymwirkung von Inosinsäure beim Glucose- und Glykogenabbau in Extrakten der Retina, *Helvet chim acta* **23** 606, 1940.

Mixtures of the acids were not as effective as adenylic acid alone, but inosinic acid did not inhibit adenylic acid

Sullmann and Bruckner<sup>79</sup> showed that glycolytic extracts of ox retinas break down glycogen chiefly via phosphorolysis. The addition of dextrose-1-phosphoric acid inhibited the phosphorylation of dextrose and of glycogen. In experiments with dextrose plus glycogen, dextrose plus dextrose-1-phosphoric acid and glycogen plus dextrose-1-phosphoric acid there was no additional lactic acid formation. Retinal extracts were able to form glycogen from dextrose-1-phosphoric acid, this reaction being accelerated by muscle adenylic acid. These authors also studied the transformation of dextrose-1-phosphoric acid to hexosediphosphoric acid.

Kerly and Bourne<sup>80</sup> noted that aqueous extracts of ox retina converted dextrose, glycogen or hexosediphosphate into lactic acid on the addition of adenosine triphosphate or adenylic acid. Adding phosphate or magnesium increased formation of lactic acid from dextrose, and the yield of hexosediphosphate was increased by magnesium but not by phosphate. After dialysis of the extract there was no formation of lactic acid from dextrose unless magnesium and phosphate were added, for formation from glycogen only phosphate, and from hexosediphosphate only magnesium, was required. In the experiments adenylic acid could replace adenosine triphosphate but with less yield, with added phosphate, however, there were greater yields of lactic acid with adenylic acid. Cozymase could not replace either adenosine triphosphate or adenylic acid. In extracts incubated with dextrose there was no evidence of phosphoric-carbonic esters. With adenylic acid used as the coenzyme there was a transfer of inorganic phosphate to an ester, probably adenosine triphosphate. With hexosediphosphate as the substrate almost all was broken down to inorganic phosphate. The incubation of dextrose with hexosediphosphate gave only slightly more lactic acid than dextrose alone.

In studying the phosphorylating glycolysis of various tissues, Meyerhof and Perdigon<sup>80</sup> found that the oxidation-reduction process between pyruvic acid and triose phosphate, formed from hexosediphosphate, was rapid in the retina, especially if hexosemenophosphate and creatine were present. The addition of a coenzymatic system, such as cozymase and adenosine triphosphate, increased the speed of glycolysis.

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<sup>79</sup> Sullmann, H., and Bruckner, R. Glykogenolyse und Glykogenbildung in Extrakten der Retina, *Enzymologia* 8 167, 1940

<sup>80</sup> Meyerhof, O., and Perdigon, E. Sur la glycolyse phosphorylante des tissus animaux, *Enzymologia* 8 353, 1940

Greig, Munro and Elliott<sup>81</sup> discovered that the oxidation in the retina was different from that in most other tissues studied in that pyruvate did not seem to be removed by the succinate-fumarate-malate-oxalacetate series. Lactate and pyruvate were oxidized rather rapidly. Succinate was oxidized only slightly to fumarate, and there was an equilibrium established between fumarate and malate, but with no further oxidation. Fumarate caused an unexplained lowering of the respiratory quotient. Acetate, formate,  $\beta$ -hydroxybutyrate, citrate and  $\alpha$ -ketoglutarate were not oxidized to any extent. This would indicate that oxidation probably does not take place through the Krebs citric acid cycle, although Krause and Stack<sup>82</sup> noted a fairly high citric acid content in the retina, which might suggest this scheme. The manometric work of Greig and associates<sup>81</sup> showed that some acid intermediate other than pyruvate was formed from lactate during the first stage of the experiment and that later, when lactate was no longer oxidized, the unknown acid acted as a substrate.

Possenti<sup>83</sup> found no, or only traces of, carboxylase in the retina and suggested that, instead of carbon dioxide being split from pyruvic acid to yield acetaldehyde, the Torriessen scheme was employed whereby two pyruvates form a diketo fatty acid, which splits into succinic and formic acids. Meyerhof and Lohmann<sup>84</sup> demonstrated the presence of zymohexase, which splits hexosediphosphate in the retina, and Elliott and Greig,<sup>85</sup> the presence of complete succinic oxidase, indophenol oxidase and succinic dehydrogenase systems in the retina. The oxygen uptake was increased to a maximum through the addition of cytochrome-C.

In the retina, Weil-Malherbe<sup>86</sup> showed that *l*-glutamic acid did not affect anaerobic glycolysis, in contrast to its inhibitory action in the

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81 Greig, M. E., Munro, M. P., and Elliott, K. A. C. The Metabolism of Lactic and Pyruvic Acids in Normal and Tumour Tissue. VI. Ocular Retina and Chick Embryo, *Biochem. J.* **33** 443, 1939.

82 Krause, A. C., and Stack, A. M. Citric and Malic Acids of the Ocular Tissues, *Arch. Ophth.* **22** 66 (July) 1939.

83 Possenti, G. Ricerche sul ricambio dell'acido piruvico nella retina, *Riv. di pat. sper.* **15** 229, 1935.

84 Meyerhof, O., and Lohmann, K. Ueber die enzymatische Gleichgewichtsreaktion zwischen Hexosediphosphorsäure und Dioxyacetonephosphorsäure. III. Ueber Abfangen der Triosephosphorsäure mit Bisulfit und die Verbreitung des Ferments, "Zymohexase," *Biochem. Ztschr.* **273** 413, 1934.

85 Elliott, K. A. C., and Greig, M. E. The Distribution of the Succinic Oxidase System in Animal Tissues, *Biochem. J.* **32** 1407, 1938.

86 Weil-Malherbe, H. Observations on Tissue Glycolysis, *Biochem. J.* **32**: 2257, 1938.

blain. Santoni<sup>87</sup> found that glutamic acid increased respiration. Greig and Munro<sup>88</sup> demonstrated that pyrophosphate had practically no effect on the normal respiration of the retina but considerably increased the rate of oxidation of glucose and lactate. By studying frozen-dried sections of the retina, Anfinsen<sup>89</sup> was able to show that the adenosine diphosphate was greater in the synaptic layers and the ganglion cell layer and less in the rods and cones.

In studying the oxidation-reduction systems in the retina, Sullmann and Schmid<sup>90</sup> found the ascorbic acid content to be 15 mg. per hundred grams (determined by titration) and that there was no difference between the light-adapted and the dark-adapted eye. Deproteinized retinal extracts gave a positive nitroprusside reaction, indicating the presence of sulfhydryl groups. Kodamari<sup>91</sup> noticed that the normal light-adapted rabbit retina contained 147.2 mg. of glutathione but that the dark-adapted retina contained 32 per cent less. Bleeding, cyanide, cocaine, ligation of the bile ducts and avitaminosis A, all conditions which decrease dark adaptation, increased the glutathione content of the retina.

Von Euler and Adler<sup>92</sup> noted the high content of flavin (evidently riboflavin) in the retina. Gourévitch<sup>93</sup> expressed the belief that the flavin content of rat retina corresponded in general to the intensity of the residual respiration. Sullmann<sup>94</sup> showed that added lactoflavin caused a loss of pyruvic acid when the mixture was illuminated.

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87 Santoni, A. Ulteriori ricerche sul metabolismo della retina, metabolismo degli aminoacidi, *Rassegna ital d'ottal* **9** 81, 1940, abstracted, *Am J Ophth* **23** 1290, 1940.

88 Greig, M. E., and Munro, M. P. Some Effects of Pyrophosphate on the Metabolism of Tissues, *Biochem J* **33** 143, 1939.

89 Anfinsen, C. B. The Distribution of Diphosphopyridine Nucleotide in the Bovine Retina, *J Biol Chem* **152** 279, 1944.

90 Sullmann, H., and Schmid, A. E. Ueber die Oxydoreduktionssysteme der Netzhaut, *Ophthalmologica* **103** 150, 1942.

91 Kodamari, S. Ueber Glutathion in der Netzhaut von Kaninchenaugen. I. Ueber den Gehalt von Glutathion in der Netzhaut bei normalen Kaninchen und einige daran anschliessende Experimente, *Acta Soc ophth jap* **39** 2053, 1935, abstracted, p. 147, II. Ueber den Gehalt von Glutathion in der Netzhaut und einiger anderer Organe bei Kaninchen unter verschiedenen Bedingungen, *ibid* **40** 2444, 1936, abstracted, p. 159.

92 von Euler, H., and Adler, E. Ueber das Vorkommen von Flavinen in tierischen Geweben, *Ztschr f physiol Chem* **223** 105, 1934.

93 Gourévitch, A. La distribution de la flavine dans les tissus des mammifères, en relation avec leur respiration résiduelle en présence des cyanures, *Compt rend Acad d sc* **204** 526, 1937.

94 Sullmann, H. Sensibilisierende Wirkung des Lactoflavins bei der photochemischen Umwandlung von Brenztraubensäure, *Klin Wchnschr* **7** 1157, 1938.

Theorell<sup>95</sup> asserted that the destruction of flavin or its ester proceeds more rapidly in the presence of oxygen and more rapidly in alkaline than in neutral mediums. Stern, Melnick and DuBois<sup>96</sup> studied the nature of Pasteur enzyme in the retina and showed it to be a pheohemin protein, similar to the respiratory enzyme in yeast and in *Acetobacter* but differing in its affinity for carbon monoxide and oxygen and in its absorption spectrum.

*Respiratory Quotient*—Dickens and Simer,<sup>97</sup> together with other investigators, concluded that the respiratory quotient of the retina was 1 and thus placed retina in the group of tissues, including brain, chorion and embryo, in which the metabolism consists strictly in the oxidation of carbohydrates. This view has been recently opposed by Elliott and Baker,<sup>98</sup> who obtained a value of 0.91 for rat retina and of 0.86 for rat brain. Possenti<sup>83</sup> obtained a respiratory quotient of 0.8 to 0.9 in Ringer's solution, which became over 1.0 when pyruvate was added.

*Fat Metabolism*—An explanation for a respiratory quotient below 1.0 may be given by recent work, which suggests the part played by a fat metabolism. Sgrosso<sup>99</sup> found in ox retina high quantities of a lipase for the low neutral fats but not for the high neutral fats. Santoni<sup>100</sup> showed that ox or rabbit retina oxidized numerous fatty acids, with the exception of formic, caproic and oleic acid. These acids inhibited the respiration. It was found that the methyl esters of the fats had a greater capacity for oxidation than the free fats. He suggested that these esters may be those normally found in the cells rather than the esters produced by the action of enzymes.

*Formation of Ammonia*—Warburg, Posener and Negelein<sup>28</sup> noticed that large quantities of ammonia were formed during anaerobic glycolysis in the retina and brain, and even larger quantities during aerobic

95 Theorell, H. Quantitative Bestrahlungsversuche an gelbem Ferment, Flavinphosphorsaure und Lactoflavin, *Biochem Ztschr* **279** 186, 1935.

96 Stern, K. G., Melnick, J. L., and DuBois, D. Nature of the Pasteur Enzyme, *Science* **91** 436, 1940. Stern, K. G., and Melnick, J. L. The Photochemical Spectrum of the Pasteur Enzyme in Retina, *J Biol Chem* **139** 301, 1941.

97 Dickens, F., and Simer, F. The Metabolism of Normal and Tumour Tissue. II. The Respiratory Quotient, and the Relationship of Respiration to Glycolysis, *Biochem J* **24** 1301, 1930.

98 Elliott, K. A. C., and Baker, Z. The Respiratory Quotients of Normal and Tumour Tissue, *Biochem J* **29** 2433, 1935.

99 Sgrosso, S. Ricerche sui fermenti lipolitici della retina, *Rinasc med* **11** 334, 1934.

100 Santoni, A. Sulla capacita del tessuto retinico di ossidare alcuni acidi grassi ed esteri metilici di acidi grassi "in vitro," *Ann di ottal e clin ocul* **67** 845, 1939, abstracted, *Am J Ophth* **23** 729, 1940.

glycolysis Rosch and te Kamp<sup>101</sup> found that retina gave off over 50 per cent of ammonia from muscle adenosine-5-phosphoric acid, 20 per cent from yeast adenosine-3-phosphoric acid, some from adenosine but none from adenine Light-adapted retina gave 5.22 mg, and dark-adapted retina 0.74 mg, of ammonia per hundred grams Lighting the dark-adapted retina increases the ammonia content at least 72 per cent. Stutzke<sup>102</sup> obtained increases of 200 to 500 per cent in ammonia content on illuminating the dark-adapted retina but no increase in the light-adapted retina Dextrose lactate or pyruvate inhibited this evolution of ammonia Rosch<sup>103</sup> observed that visible light and roentgen rays of long medium wavelength, but not ultraviolet rays, caused the evolution of ammonia, in proportion to the intensity of light Dickens and Greville<sup>104</sup> found production of ammonia to be small in the retina, but in the absence of dextrose or fructose it became large relative to the respiratory rate, partly because of the large fall in the latter

*Glycogen*—The presence of glycogen in the retina has been a subject of some dispute Ehrlich,<sup>105</sup> in 1833, detected glycogen in frog retina, and Luna,<sup>106</sup> Muller<sup>107</sup> and others found it in other animals Best<sup>108</sup> and Matsuoka<sup>109</sup> claimed that the normal retina was free of glycogen, but Schmitz-Moormann,<sup>110</sup> with careful staining, demonstrated glycogen in the inner segment in the base of the cones and in the myoid

101 Rosch, H., and te Kamp, W. Ueber Ammoniakbildung bei Belichtung der Netzhaut, *Ztschr f physiol Chem* **175** 158, 1928

102 Stutzke, S. Ueber die Ammoniakbildung in der Netzhaut, *Klin Wchn-schr* **15** 524, 1936

103 Rosch, H. Weitere Untersuchungen uber die Ammoniakbildung in der Netzhaut, *Ztschr f physiol Chem* **186** 237, 1930

104 Dickens, F., and Greville, G. D. The Metabolism of Normal and Tumor Tissue IX. Ammonia and Urea Formation, *Biochem J* **27** 1123, 1933

105 Ehrlich, P. Ueber das Vorkommen von Glykogen im diabetischen und im normalen Organismus, in Frerich, F. T. Ueber den plotzlichen Tod und uber das Coma bei Diabetes, *Ztschr f klin Med* **6** 3, 1833

106 Luna, E. Ricerchi istologiche e istochimiche sulla retina dei vertebrati, *Monitore zool ital* **22** 119, 1911

107 Muller, C. Das Glycogen der Retina des Frosches, *Ztschr f d ges Anat* **81** 220, 1926

108 Best, F. Demonstration mikroskopischer Präparate vom diabetischen Auge, *Ber u d Versamml d deutsch ophth Gesellsch* **32** 315, 1906, Die Bedeutung des pathologischen Glykogengehaltes, *Zentralbl f allg Path u path Anat* **18** 465, 1907

109 Matsuoka, J. Ueber das Glykogen in der Netzhaut, *Nippon Gankwa Gakkai Zasshi* **23** 1919, cited by Schmitz-Moormann<sup>110</sup>

110 Schmitz-Moormann, P. Ueber der Glykogengehalt der Retina und seine Beziehungen zur Zapfenkontraktion, *Arch f Ophth* **118** 506, 1927

but not in the rods Fontana<sup>111</sup> saw glycogen granules in the pigment epithelium, in the cones and in the external limiting membrane There was no glycogen in the pigment epithelium if the eyes were kept in the dark, but much in bright light the other deposits of glycogen remained unchanged Brammertz,<sup>112</sup> on the other hand, detected in the eye of the housefly an increase of glycogen in the dark-adapted eye and a decrease in the light-adapted eye

Best<sup>113</sup> found that ocular inflammations subconjunctival injections of a 10 per cent solution of sodium chloride, subcutaneous injections of phlorhizin and diabetes increased the retinal glycogen Majima<sup>9</sup> and Nakayasu<sup>114</sup> noted that epinephrine increased the glycogen Nakayasu also found that the injection of 10 units of insulin per kilogram produced a fall or disappearance of glycogen in the retina, 5 units a slight reduction and  $\frac{1}{2}$  unit a rise Thyroxin or thyroid extract produced a rise of glycogen, as also did solution of posterior pituitary U S P Trematori<sup>115</sup> investigated the amylase of the retina and found it to have an optimum of  $p_H$  of 7.8 and an optimum sodium chloride concentration of 0.008 to 0.013 per cent Fluoride completely inhibited, and hydrogen peroxide and formaldehyde partially inhibited, the amylase

*Carbon Dioxide Anhydrase*—Bakker<sup>116</sup> found a high concentration of this enzyme in the retina and lens, some in the cornea and choroid and none in the sclera He assumed that tissues with a high aerobic glycolysis and a paucity of blood vessels need a high concentration to catalyze the rapid dissolution of carbon dioxide He<sup>117</sup> showed that carbon dioxide anhydrase produced both a hydration and a dehydration of carbon dioxide, although in the retina dehydration occurs more readily than hydration The reaction was activated in both directions by cysteine, histidine, histamine and glutathione

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111 Fontana, G. Ulteriori ricerche istologiche sul glicogeno della retina di alcuni vertebrati allo stato normale ed in talune condizioni sperimentali, *Rassegna ital d'ottal* **4** 135, 1935

112 Brammertz, W. Ueber das normale Vorkommen von Glykogen in der Retina, *Arch f mikr Anat* **86** 1, 1914

113 Best, F. Beitrag zur Wirkung subconjunctival Injektionen, *Arch f Augenh* **57** 173, 1907, footnote 108

114 Nakayasu, S. Ueber den Einfluss der verschiedenen Präparate der inneren sekretorischen Organe auf den Glykogenstoffwechsel in der Netzhaut, *Acta Soc ophth jap* **37** 941, 1933, abstracted, p 71

115 Trematori, M. L'amilasi della retina, *Riv biol* **20** 108, 1936

116 Bakker, A. Der Kohlensäureanhydrasegehalt verschiedener Augengewebe einiger Säugetiere, *Ophthalmologica* **102** 351, 1941

117 Bakker, A. Bewirkt die Kohlensäureanhydrase in den Augengewebe eine Hydratation von Kohlendioxyd oder eine Dehydratation von Kohlensäure? *Ophthalmologica* **103** 88, 1942

*Acetylcholine*—Lange<sup>118</sup> found that after dark adaptation 20 frog retinas (0.5 Gm) contained 150 micrograms of acetylcholine, while after light adaptation the same number contained only 15 micrograms. Similar results on the effect of light were obtained by Chang, Hsieh, Lee and Li,<sup>119</sup> Nakashima and Murata,<sup>120</sup> and Chang, Lee and Li.<sup>121</sup> Bakker<sup>122</sup> demonstrated the formation of acetylcholine in the retina by noticing the action of an explanted iris when the retina was also explanted. Anfinson<sup>123</sup> demonstrated that cholinesterase occurred chiefly in the synaptic layers of the retina.

*Detached Retina*—By studying the special metabolism of the detached retina, some clues may be obtained as to normal retinal metabolism. Weve and Fischer<sup>124</sup> showed that, while normal retina in contact with the pigment epithelium has a low oxidation-reduction potential, the detached retina was more highly oxidized, this oxidation being evidently due to an alteration in its metabolism. On detachment it was no longer glycolysis, but respiration, which prevailed. Glycolysis and vision seemed to depend on the contact of retina with pigment epithelium. Fischer<sup>125</sup> showed the detached retina to be more acid. Weve and Fischer<sup>126</sup> demonstrated a high amylase content of the subretinal fluid, liberated as a result of autolysis of retinal cells and not due to any admixture of blood. Amylase was found to occur

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118 Lange, V. Ueber das Vorkommen von Acetylcholin im hell- und dunkel-adaptierten Auge, *Ztschr f physiol Chem* **279** 73, 1943, abstracted, *Chem Abstr* **38** 3024, 1944.

119 Chang, H., Hsieh, W. M., Lee, L. Y., and Li, T. H. Diminution of Acetylcholine Content of Retina After Prolonged Functional Disuse, *Proc Soc Exper Biol & Med* **43** 140, 1940.

120 Nakashima, M., and Murata, G. Ueber die Cholinmenge der Hell- und Dunkelnetzhaut, *Acta Soc ophth jap* **43** 660, 1939, abstracted, p. 41.

121 Chang, H. C., Lee, L. Y., and Li, T. H. Tissue Acetylcholine. IX. Diminution of Acetylcholine of Retina During Functional Disuse, *Chinese J Physiol* **16** 373, 1941.

122 Bakker, A. Ueber Acetylcholinbildung in der Retina, *Arch f Ophth* **141** 326, 1939, abstracted, *Chem Abstr* **34** 3801, 1940.

123 Anfinson, C. B. The Distribution of Cholinesterase in the Bovine Retina, *J Biol Chem* **152** 267, 1944.

124 Weve, H. J. M., and Fischer, F. P. Le métabolisme de la rétine décollée, *Ann d'ocul* **175** 817, 1938.

125 Fischer, F. P. Metabolismus der abgelosten Netzhaut, *Nederl tijdschr v geneesk* **83** 4187, 1939, abstracted, *Zentralbl f d ges Ophth* **44** 395, 1939.

126 Weve, H. J. M., and Fischer, F. P. Ueber die Amylase der subretinalen Flüssigkeit, *Arch f Augenh* **110** 390, 1937.



only in the retina<sup>127</sup> A high acetylcholine esterase content was observed in subretinal fluid<sup>128</sup>

#### COMMENT

The foregoing evidence is not sufficient to allow one to outline an integrated framework of retinal metabolism, yet one may list, without attempting to connect, some of the important reactions in accordance with the weight of the evidence, as few facts stand completely unopposed

On stimulation with light, acetylcholine is liberated in the retina, this perhaps being the substance which stimulates the nerve elements, phosphocreatine is converted into creatine and phosphoric acid, and adenosine triphosphate is split into the diphosphate and phosphonic acid, in addition to the fundamental conversion of rhodopsin into other products The decomposition of phosphocreatine and adenosine triphosphate results in the liberation of energy, possibly both reactions occurring in a stepwise fashion The energy, then, for the reformation of rhodopsin, phosphocreatine, adenosine triphosphate and perhaps other substances as well as the basal energy requirements of the cells comes largely from the oxidation of glucose The effect of poisons and substrates and of added enzyme systems and the determination of intermediate products would indicate that glycolysis follows a scheme similar to that of muscle glucose through the hexosemonophosphates to hexosediphosphate, thence to dioxycetone phosphate and glyceraldehyde phosphate followed by oxidization to phosphoglycerate and then pyruvate, which yields lactate and is eventually oxidized to carbon dioxide and water The intermediate substances are not all known but it may be supposed that the entire Cori scheme is reproduced, and it seems likely that the Krebs citric acid cycle is employed The Pasteur effect is present Glycogen which is probably stored in the normal retina, may supplement blood glucose Certainly the metabolism, primarily glycolytic, may also involve the oxidation of fats and amino acids, with resulting respiratory quotients below 1

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127 Weve, H J M Der Enzymgehalt der retroretinalen Flüssigkeit, *Nederl tijdschr v geneesk* **81** 3000, 1937, abstracted, *Zentralbl f d ges Ophth* **39** 367, 1937

128 Weve, H J M, and Fischer, F P Ueber den Azetylcholinesterase-Gehalt der subretinalen Flüssigkeit bei rupturellen Netzhautablosungen, *Ophthalmologica* **96** 348, 1939

## Obituaries

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### ANDREW MAITLAND RAMSAY, M D 1859-1946

Dr Maitland Ramsay died at his home in St Andrews, Scotland, on March 20, at the age of 86. After receiving his medical education at the University of Glasgow and at the Western Infirmary, he entered general practice and was particularly active in the Charlotte Street Dispensary of the Glasgow Eye Infirmary. In 1898 he was appointed surgeon to the Ophthalmic Institution, which was the eye department



ANDREW MAITLAND RAMSAY, M D  
1859-1946

of the Glasgow Royal Infirmary, an institution founded by J R Wolfe, whose name is known in connection with skin grafting. Dr Ramsay was instrumental in the foundation of a chair in ophthalmology in the University of Glasgow with a bequest given by L Gavin Tennent, his friend and teacher, whose bequest also included the construction of the Tennent Memorial Eye Institute.

Dr Ramsay wrote a number of important books, such as "Atlas of External Diseases of the Eye," 1898, "Eye Injuries and Their Treatment," 1907, "Diathesis and Ocular Diseases," 1909, "Clinical Ophthalmology for the General Practitioner," 1920, and "The Eye in General Medicine," 1929. The titles of these books show that Dr Ramsay approached his subject from the standpoint of general medicine. He took every opportunity of encouraging the use of the ophthalmoscope by the internist in the routine examination of his patients and always stressed the close association of ocular disorders and general diseases. Dr Ramsay was fundamentally a clinical ophthalmologist, following in the tradition of his great predecessor, William Mackenzie. His interest in general medicine remained throughout his life, and he was convinced that the physician's chief duty lay in clinical observation, rather than in dependence on laboratory investigations.

In 1904 Dr Ramsay attended the annual meeting of the American Medical Association and delivered an address on "The Importance of General Therapeutics in the Treatment of Ocular Diseases."

He retired at the age of 60 and settled at St Andrews, where, with his wife, who was Dr Elizabeth Margaret Pace, he lived many happy years and gave much pleasure to those who were fortunate enough to enjoy his hospitality. At the same time he continued his interest in medicine, particularly the investigations that were being carried out in the institution founded by Dr James Mackenzie.

Tall, of distinguished appearance and gentle manners, Dr Ramsay endeared himself to patients and colleagues alike. He had firm convictions and views, which he did not hesitate to express, and he was much distressed with the trend of modern medicine. In his last address, "The Making of the Family Doctor," dedicated to the medical students of St Andrews University, he concluded with the statement that the state can never replace the relationship between the physician and his patient and insisted that it is not possible to buy research on a large scale.

ARNOLD KNAPP

# Abstracts from Current Literature

EDITED BY DR WILLIAM ZENTMAYER

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## Anatomy and Embryology

SIMILARITY OF THE DEVELOPING RETINA AND BRAIN WALL IN HUMAN EMBRYOS H C HADEN, *Am J Ophth* 28:943 (Sept) 1945

Haden explains the embryonic similarity of the retina and the wall of the brain by means of eighteen illustrations of sections from human embryos

W S REESE

## Aqueous Humor

ROENTGENOLOGIC STUDY OF OUTFLOW OF THE AQUEOUS M BALTIM, *Vestnik oftal* 24:14, 1945

The basis for this study was the introduction into the anterior chamber of contrasting substances and the follow-up observation on the paths of their outflow in the roentgenograms

Baltin tried injection of iodized poppyseed oil, seigoin and solution of 20 per cent potassium iodide in rabbit eyes, but none of these substances could be traced. He then used Thorotrast (a colloidal solution of thorium dioxide). After emptying the anterior chamber, 0.1 or 0.2 cc of the substance was introduced with the same needle. A roentgenologic examination was made every half-hour on the day of the injection and then daily during the time of the observation. The dye could be followed up to the suprachoroidal space. The rabbit eyes were enucleated at various intervals. Histologic examination on the second day showed the presence of round cells in the angle of the anterior chamber, in Fontana's spaces, in the ligamentum pectinatum and in the ciliary body, there were a large number of cells also at the pupillary margin of the iris. Schlemm's canal was free from the cells. These cells contained the thorium dioxide.

Thorotrast was introduced into eyes in which atropine and physostigmine were instilled, as well as into glaucomatous eyes. Roentgenologic examination showed no change in any of these eyes as compared with the normal.

Baltin summed up his experimental work as follows:

1. Roentgenologic examination of 40 rabbit eyes showed the gradual absorption of the dye and its passage from the angle of the anterior chamber into the suprachoroidal space. Dye was also present on the iris but not in Schlemm's canal, the last factor may lead one to believe that the outflow of the aqueous is accomplished not by filtration but by more complex processes, which are not known at present.

2. The cells which absorb the thorium dioxide belong to the group of macrophages and are called histiocytes. They absorb various colloidal substances introduced into the organism.

3. The roentgenologic method makes it possible to follow in the living eye the passage of substances introduced from outside into the eye. However, since the conditions are not similar to those under normal physiologic conditions, it is not the best way.

O SITCHEVSKA

## Blind

FUNCTIONAL BLINDNESS IN WARTIME (DIAGNOSIS AND TREATMENT)  
Z KOPUL-LEVINA and O SIERSHEWSKAYA, *Vestnik oftal* 23: 31,  
1944

The case histories of 8 patients with functional blindness are reported

A private aged 43 lost vision as a result of contusion of the brain and simultaneous trauma of the face with shrapnel. There was also loss of hearing and speech. The patient was stuporous. The diagnosis of functional blindness was established by the presence of analgesia of the lids and normal media and fundi. Psychotherapy as well as hypnosis gradually brought back the vision and hearing and, as a result, improvement in the tone of the central nervous system and return to normal life after four months of hospitalization.

A private aged 48 received a contusion by air waves in the explosion of an aviation bomb. He was unconscious for four hours, after which there were vomiting, nausea, severe headache and loss of hearing, speech, vision and motion. Speech and hearing in the left ear were restored shortly after the contusion, but general asthenia, blindness and loss of hearing in the right ear remained stationary. There was an area of analgesia of the lids and orbit in the shape of spectacle lenses. The media and fundi were normal. The behavior of the patient was of the reactive depressive type. Hypnosis and psychotherapy were instituted, after the first treatment vision was 0.1 in each eye, and within four weeks it was 0.7 in the right eye and 0.8 in the left eye. The general condition improved also.

In 2 privates, aged 30 and 20, respectively, there was concentric contraction of the visual fields after contusion, in the younger patient there were also deaf-mutism and incontinence of the urine. Partial analgesia of the lids was present in both cases. Psychotherapy aided in the restoration of the visual fields to normal.

The diagnosis of functional blindness was made because of analgesia of the region of the lids in the shape of spectacle lenses. Hypnosis and psychotherapy usually give good results.

O SITCHEVSKA

## Conjunctiva

CHRONIC CONJUNCTIVITIS OF THE INTERNAL ANGLE CONSEQUENT TO  
IGNORED CANALICULAR MYCOSIS. A VAZQUEZ BARRIÈRE and  
R. V. TALICE, *Arch de oftal de Buenos Aires* 19: 1 (Jan) 1944

Chronic conjunctivitis involving the bulbar conjunctiva in the region of the internal angle which does not respond to treatment may be produced by unsuspected mycosis of the lacrimal canaliculi.

A case is reported in which such a condition occurred. On careful examination it was found that a zone of congestion surrounded the upper punctum, which was open and dilated. Yellow concretions were extracted from the canaliculus, which when examined microscopically showed the presence of the mycelium of *Actinomyces*.

H. F. CARRASQUILLO

A GRAVE TYPE OF PURULENT CONJUNCTIVITIS OF THE NEWBORN.  
A VILACORO, Arch Soc oftal hispano-am 4: 18 (Jan-Feb) 1944.

The disease makes its appearance three or four days after birth, with moderate conjunctival congestion. In three days purulent conjunctivitis sets in, with intense congestion of the bulbar and palpebral conjunctiva and abundant discharge over the lids. Two or three days later the inflammation reaches its maximum, and the chemotic conjunctiva shows over the margins of the lids, which are red and swollen. At this time superficial infiltration of the cornea is observed. Ultimately, the entire thickness of the cornea is involved. Perforation may take place. When the condition subsides, the cornea remains opaque, and vision is greatly limited or altogether lost.

All efforts to find the causative agent of the disease have failed. No bacteria or inclusion bodies have been identified. It is thought that some filtrable virus may be responsible.

Treatment is of no avail. The disease lasts two or three months. The author reports 4 cases. Complete blindness resulted in 2 of the cases and partial blindness in the other 2 cases.

H F CARRASQUILLO.

### Congenital Anomalies

DERMAL LIPOMA OF THE CONJUNCTIVA WITH SCLERAL CYST AND  
COLOBOMA OF THE PALPEBRAL ANGLE W B MATTOS, Arq brasil  
de oftal 5: 39 (April) 1942

The author presents a clinical observation on a patient 7 years of age. Examination showed a greatly widened palpebral fissure, due to a coloboma of the external angle. In the latter region a large, yellowish rose tumor covered more than half the cornea and extended into the outer portion of the upper and lower cul-de-sacs, preventing the patient from closing the eye. The eye was turned inward, and its movements were much reduced.

Operation was performed, with subconjunctival ablation of the tumor. The conjunctiva was spared as much as possible, the tumor being disinserted from the cornea, to which it was closely adherent. The tumor was dissected along its whole length between the superior, internal and inferior rectus muscles. In the region of the inferior rectus, a scleral cyst was found at 5 o'clock, just behind the limbus. This was not removed but was left for a future operation. As strabismus was present, tenotomy of the internal rectus muscle was performed. At a second operation the scleral cyst was removed and the palpebral coloboma closed. A slight convergent strabismus and a leukoma over one-half the cornea remained.

The author was unable to find any reference in the literature on epibulbar tumors associated with scleral cyst.

M E ALVARO

CONGENITAL ANIRIDIA REPORT OF A CASE H MARBACK, Arq.  
brasil de oftal 5: 97 (June) 1942

The author presents a case history.

A man aged 20, with no family history of any ocular defect, showed horizontal nystagmus, which increased involuntarily in a strong light.

01 when the patient tried to fixate objects in distant or near vision. There was complete absence of the iris in both eyes, resulting in an excessively large pupillary orifice, the limit of which was determined by the contour of the cornea, which was of normal size. The cornea was transparent, except in the lower limbal region, where there was a partial embryotoxon. The lens was semidislocated and rotated upward and backward, completely opacified and of a grayish white color. The fundus was normal. In each eye visual acuity taken with a +13 D sphere was limited to counting fingers at 3 meters. This acuity was relatively good for a case of this kind and in accord with the normal aspect of the fundus, as in the great majority of cases aniridia is associated with absence of the macula.

The author agrees with Duke-Elder that two different mechanisms may produce the same anomaly. 1 Aniridia may result from lack of development of the retinal ectoderm at the level of the edge of the optic vesicle. That aniridia is always associated with other ectodermal defects supports this theory. 2 The anomaly may be the result of a malformation of the vascular mesoderm, due to a mechanical obstruction in the development of the iris, caused by remnants of the fibrovascular capsule of the lens.

M E ALVARO

### Experimental Pathology

PIGMENTARY MOBILIZATION PROVOKED BY LESION OF THE CERVICAL SYMPATHETIC GANGLION. R RODRIGUEZ BARRIOS, Arch de oftal de Buenos Aires 18:709 (Dec) 1943

In the course of a series of experiments to ascertain the action of the sympathetic nervous system on the eye, Rodriguez Barrios observed the following phenomenon. A few days after extirpation of the superior cervical ganglion, mobilization of pigmentary cells (melanophores) was observed. Invasion of the periphery of the cornea by these cells appeared four days later and progressed, forming an annular zone, which reached a width of 2 mm in some places.

The observation is reported in the hope that further experiments will be carried out on this line of investigation.

H F CARRASQUILLO

### General Diseases

MARFAN'S SYNDROME. C H JOLLY and O H SOLA, Arch de oftal de Buenos Aires 18:697 (Dec) 1943

The authors report a clinical case of the disease in a boy aged 14, who was 185 meters (72½ inches) tall and weighed only 60 Kg (130½ pounds). Exaggerated height and obesity occurred in his ancestors.

The abnormal length of his hands and feet was conspicuous. Clinical and roentgenographic examinations of his hands showed arachnodactyly. There was no abnormality of the heart. Ocular examination demonstrated the presence of bilateral ectopia of the crystalline lens. With corrections of +4.00 D sph for the right eye and a +7.00 D sph for the left eye vision was 1/2 to 1/10 in the respective eyes.

H F CARRASQUILLO

OPHTHALMOPATHIES OF TUBERCULOUS ORIGIN P FILHO, Arq brasil de oftal 5:101 (June) 1944

The author first discusses syphilis and focal infections, pointing out that these disease processes cause lesions similar to those of tuberculosis and that, instead of one's being so ready to make a diagnosis of syphilis, tuberculosis should be considered more often

Patients with ocular tuberculosis often show no general symptoms, tuberculosis rarely being apparent in other parts of the body The various tests for the diagnosis of tuberculosis are discussed, their value being doubtful, as a low degree of sensitivity to tuberculin and lack of other clinical signs are noted sometimes in patients with old tuberculosis Torpid uveitis, especially that occurring after operation, is discussed, and 2 cases of the latter type are reported Sympathetic ophthalmia and Boeck's sarcoid are also discussed M E ALVARO

### **Glaucoma**

LATE RESULTS OF CYCLODIALYSIS FOR GLAUCOMA N IVANOV, Vestnik oftal 24:66, 1945

Cyclodialysis was suggested by Heine in 1905 for relief of chronic glaucoma as a means of establishing a connection between the anterior chamber and the suprachoroidal space

The results of cyclodialysis were observed in 100 patients The period of observation was from two to five years for 87 patients and from five to eight years for 13 patients The tension, visual acuity and visual fields were tested periodically in the Moscow University Eye Clinic Fifty-one patients had chronic inflammatory glaucoma, 45 simple glaucoma and 4 secondary glaucoma

A detailed analysis of the cases is given Ivanov believes that cyclodialysis is a safe operation, with no complications as a rule, the earlier it is done, the better is the chance of obtaining improved vision, visual fields and tension His conclusions are as follows

1 Cyclodialysis was performed on 100 patients with glaucoma, the time of observation being from two to eight years Intraocular tension became normal in 70.6 per cent of patients with chronic inflammatory glaucoma and in 51.1 per cent of patients with simple glaucoma

2 The visual acuity remained unchanged in 39.2 per cent of patients with chronic inflammatory glaucoma and in 17.7 per cent of patients with simple glaucoma In 26 per cent of patients blindness followed, and in 18 per cent cataract developed

3 Cataract develops in hypotonic eyes as a result of postoperative changes in the ciliary body

4 The visual fields remained unchanged in 60.8 per cent of patients with chronic inflammatory and in 31 per cent of patients with simple glaucoma

5 Myopia developed in 11 per cent of emmetropic and hyperopic eyes and increased in 3 per cent of myopic eyes

O SITCHEVSKA



## Injuries

CHOLINESTERASE CONTENT OF THE EYE R Bruckner, *Ophthalmologica* 105 37-49 (Jan) 1943

Bruckner presents investigations on the presence and importance of cholinesterase in the eye, particularly in the aqueous humor and the vitreous body. Studies on horses and cows revealed that cholinesterase is a regular constituent of the aqueous humor, and it is assumed that this is the case also in man. The esterase found in the aqueous probably is derived not from the blood but from other sources. The esterase values of the vitreous body of cows, calves and hogs were several times as high as those of the aqueous humor, in cows it was four times as high as in the serum, in horses the esterase values of the vitreous body were occasionally lower than those of the aqueous. In cows the concentration of esterase varied in the different parts of the vitreous, it was greatest in the peripheral zones. The esterase of the vitreous body is probably derived chiefly from the retina.

J A M A (W ZENTMAYER)

TREATMENT OF WAR BLINDNESS P TIKHOMIROV, *Vestnik oftal* 28. 10, 1944

Blindness in wartime is due chiefly to perforating injuries of both eyes, which are severer than injuries in peacetime. They consist of injury to the cornea and sclera, prolapse of the iris, traumatic cataract and large tears in the choroid and retina. Contusions are the second most frequent cause of blindness. Frequently the blindness in one eye was due to a perforating injury and in the second to blunt trauma. According to the statistics of several military hospitals, bilateral injury of the eyes is met with in 15 per cent of all cases of ocular injuries. Tikhomirov divides into four types the complications resulting from injuries in which treatment may restore vision, namely, traumatic cataract, opacities of the cornea, detachment of the retina and hemophthalmos.

His first group consisted of cases of injury to the lens. In 67 per cent traumatic cataract was observed in the only remaining eye (the second eye was enucleated), and in 33 per cent of cases the second eye was normal. Only in 17 per cent of cases was there no complication. In 83 per cent the following complications occurred: foreign bodies, both magnetic and nonmagnetic, in the episclera, the cornea, the ciliary body and the posterior part of the eye, posterior synechia, and corneal opacities. When the cataract became tumescent and caused glaucoma, a linear extraction of the lens normalized the tension. As a rule extraction of the cataract was done within one to two months of the injury, but when there was but one eye the operation was done after all danger of infection from the conjunctiva, the tear sac and foci of infection was eliminated. In some cases immediately after the extraction the magnet was used for removal of the intraocular foreign body. In some eyes the foreign body (at times multiple) could be seen in the eye long after the extraction was done, but the eyes remained quiet over long periods of observation. Cataract formed always as the result of perforating trauma of the eye.

The second group consisted of cases of corneal opacities, frequently the result of injury by mines. Total leukomas with anterior and posterior synechias often were complicated with secondary glaucoma. A number of operations for glaucoma must be performed at times in order to stabilize the tension. The most effective proved to be Vogt's method—diathermy coagulation of the ciliary body. In 10 eyes a corneal transplantation was done, and in 1 eye with dense opacities keratoplasty was done five times before any vision was obtained.

The third group consisted of cases of retinal detachment—those in which the lesion was caused by retinitis proliferans and the prognosis was usually poor and those in which a tear was found. In these cases diathermy was usually successful. A military physician had received bilateral perforating injuries of the eyes with glass. After five operations for traumatic cataract total retinal detachment developed in the right eye and a partial detachment in the left eye. Two operations resulted in restoration of ability to count fingers in the left eye only.

The fourth group consisted of cases of intraocular hemorrhage. Hemorrhage into the eye is frequently the cause of blindness in cases of ocular injuries because the blood organizes and produces retinitis proliferans and retinal detachment. With conservative treatment the hemorrhages may absorb within five to six months. The treatment should be started early with evacuation of the blood.

Thus, Tikhomirov believes that the treatment of blindness due to war injuries results in improvement of vision. The methods may vary, but persistence on the part of physician and patient and a number of operations may restore at least partial vision.

O SITCHEVSKA

### Instruments

THE STANDARDIZATION OF SO-CALLED SCHIÖTZ TONOMETERS P C KRONFELD, *Am J Ophth* 28.34 (Jan) 1945

Kronfeld discusses standardization of tonometers and concludes that the method of standardization by measuring the physical properties is sound.

W S REESE

NEW PERMANENT HAND MAGNET IN THE LIGHT OF PRESENT DAY MAGNET-OPERATION METHODS B S BRODSKY, *Am J Ophth* 28: 1245 (Nov) 1945

Because of the inconvenience of the giant magnet, Brodsky devised a permanent magnet made of iron, nickel and aluminum and the alloy Alnico. He describes his method in cases in which a magnet was used in extraction.

W S REESE

### Methods of Examination

FALT'S TEST FOR ESTABLISHING UNILATERAL BLINDNESS, MARKED DECREASE OF VISION OR MALINGERING M M BALTIM, *Vestnik oftal* 23.22, 1944

The test is made as follows. The subject is asked to fix the approaching finger or light at 15 cm. As the finger comes closer, the

blind or poorly seeing eye starts to diverge, if both eyes see, normal convergence will be maintained. With this test a unilateral paralysis of accommodation can also be established.

Baltin has used this test for many years and confirms Falt's claims for its usefulness. The test is simple and needs no instruments, it does not depend on the intelligence of the subject, it aids in determining not only unilateral blindness but pronounced reduction of vision. Malingering is fully established. If the test gives a positive result, it is usually impossible to correct the vision. It can be demonstrated to outside observers.

O SITCHEVSKA

### Neurology

OCULAR NEUROVEGETATIVE SYSTEM. BLUE EYES AND BROWN EYES  
F VIDAL and C S. DAMEL, Arch de oftal de Buenos Aires 18 593  
(Nov) 1943

Studies made on the neurovegetative system of the eye have proved that in man the sympatheticomimetic drugs act better and in lesser concentration in subjects with light-colored irises.

The author made observations on 200 persons with minor refractive errors, of both sexes and of ages ranging from 5 to 64 years and having apparently normal neurovegetative systems. One patient with heterochromia was included. Fourteen of the subjects tested showed neurovegetative dystonia.

The drugs used were 1 per cent phenylisopropylamine sulfate and 5 per cent *l*- $\alpha$ -phenyl- $\beta$ -2-methylaminopropanol sulfate. The same number of drops were instilled in the upper limbus in each subject. The experiments showed clearly that sympatheticomimetic drugs act better and in weaker concentrations in persons with light-colored eyes.

The action is greatest in eyes with blue irises and next in eyes with greenish, greenish brown and brown irises, in that order. In the dark brown eyes the effect is slight. In the patient with heterochromia the effect was pronounced on the bluish gray iris. In the subjects with neurovegetative dystonia the drugs acted without any relation to the color of the iris.

H F CARRASQUILLO

OCULAR CHANGES IN FIFTY CASES OF GENERAL PROGRESSIVE PARALYSIS. E ANDROGUE and J TELTAMANTE, Arch de oftal de Buenos Aires 19.8 (Jan) 1944

Fifty cases of general progressive paralysis were studied in relation to their ocular changes. Disturbances of the photomotor reflex were exhibited in 68 per cent of cases. The Argyll Robertson pupil was present in 20 cases, in 10 of which the pupils were miotic, in 5 normal and in 5 mydriatic. In 6 per cent there was total pupillary rigidity. In all cases the action on the iris of pilocarpine, homatropine, physostigmine and atropine was evident.

H F CARRASQUILLO

OPTICOCIASMIC ARACHNOIDITIS. A ANDROGUE and M DIEZ, Arch de oftal de Buenos Aires 19 20 (Jan) 1944

A statistical study of the symptomatology of this condition was made, with the purpose of evaluating each symptom. Forty cases were

analyzed in which operation was performed, and a synopsis of the clinical and laboratory data in each case is given

Males predominated (65 per cent) The ages ranged from 13 to 62 years, most of the patients being between 13 and 45 years of age

Syphilis and trauma were the causative factors in 50 per cent of the cases Intrinsic motility was preserved in 52.5 per cent, and the reflexes were disturbed in 18 per cent Optic nerve atrophy was present in 52.5 per cent Visual acuity was diminished in 85 per cent In the field study, scotomas were present in 37.5 per cent of cases and a concentric contraction in 30 per cent In 29 cases the diagnosis was proved by exploration of the chiasmic region, and in 10 cases, by subtemporal decompression, in 2 cases the diagnosis was made clinically

Early surgical treatment is advocated H F CARRASQUILLO

### Ocular Muscles

SUMMARY OF REEXAMINATION OF ORTHOPTIC PATIENTS WITH CONSIDERATION OF PERMANENCE OF RESULTS J S ROBINSON, *Am J Ophth* 28: 999 (Sept) 1945

Robinson concludes (1) that the potential response of each patient is a deciding factor in the permanent result, (2) that the limitations of orthoptic treatment must be realized and (3) that with such therapy the tendency of an eye to deviate is often not eliminated but, rather, the ability to overcome this tendency is strengthened so that the deviation is not troublesome Finally, he states that a good result depends on correct diagnosis and proper treatment by various methods in logical sequence

W S REESE

RESECTION OF THE INFERIOR OBLIQUE MUSCLE IN HYPOTROPIA O H WAGMAN, *Am J Ophth* 28: 1220 (Nov) 1945

Wagman discusses resection of the inferior oblique muscle in cases of this imbalance and emphasizes the necessity of proper work-up of such cases He reports a case in which he resected the inferior oblique, did a recession of the rectus internus and resected the rectus externus muscle

W S REESE

INVERTED BELL SIGN M MARIN AMOT, *Arch Soc oftal hispano-am* 4: 534 (July-Aug) 1944

A case of an inverted Bell sign is reported When the eyes were closed, the globe was turned down instead of moving upward, as in the usual Bell phenomenon, the synergy occurring between the closing of the lids and the depression of the eye

H F CARRASQUILLO

### Orbit, Eyeball and Accessory Sinuses

OPTICAL IRIDECTOMY ON SUBATROPHIC EYES A VON FILATOV, *Vestnik oftal* 24: 8, 1945

Filatov reports 2 cases of war injury of the only eye in which optical iridectomy was done, with resulting ability to count fingers He believes

that even in the presence of faulty light perception only the ophthalmologist should not give up and should give the patient the benefit of minimum vision, which is better than none

Tissue therapy in the form of injections of preserved placenta tissue was given the patients for months before and after the operation

O SITCHEVSKA

#### ENUCLEATIONS IN WARTIME C PTITZA, Vestnik oftal 24 74, 1945

During 1942 and 1943 714 operations on the eye were performed in the evacuation hospital. Of these, 52.3 per cent were penetrating ocular injuries, and the proportion of enucleations was high. 195 enucleations and 72 eviscerations. The enucleations of wartime differ from those of peacetime. The eyeball is frequently "smashed", later, firm adhesions form with the muscles and orbit. Fragments are frequently found, and there are infected wounds near the eyeball, all of which factors make enucleation in wartime difficult and often dangerous, as it may be complicated by phlegmon, sinus thrombosis and meningitis. The author reports 2 cases of meningitis which followed enucleation in the absence of any clinical contraindications. Frequently fragments were removed when cutting the optic nerve, sometimes it was necessary to remove the fragments after the enucleation.

Sulfanilamide powder was always used for the conjunctival wound, and sulfonamide preparations were administered internally. In cases of wounded service men with serious general wounds, fever and undernourishment, enucleation was usually postponed until the general condition was improved. Enucleation was done in a few cases of injury to the skull with low grade meningoencephalitis, no complications were encountered.

O SITCHEVSKA

#### Refraction and Accommodation

##### TRANSIENT MYOPIA DURING TREATMENT WITH SULFANILAMIDE C BRITTO, Arq brasil de oftal 5:35 (April) 1942

The author presents a clinical observation on a patient who had taken 2 Gm of sulfanilamide daily for eight days. At the end of this period headache, vomiting and loss of appetite appeared and the treatment was suspended, myopia being noted soon after. Visual acuity without correction was 1/2 in each eye. Homatropine had no effect on refraction. The myopia gradually decreased, and eight days after the first examination visual acuity was 20/20, without correction.

A tabulation of 20 cases reported in the literature is presented. The various theories regarding pathogenesis are discussed, the author being inclined to accept that of spasm of accommodation.

A bibliography is included.

M E ALVARO

#### Retina and Optic Nerve

##### PHOTO-RETINITIS IN ANTI-AIRCRAFT LOOKOUTS JAMES FLYNN, M J Australia 2 400 (Oct 31) 1942

The author, a surgeon lieutenant commander with the Royal Australian Navy, observed that watchers at antiaircraft look-outs and similar

personnel have frequently to look directly into the sun. Four cases of photoretinitis in such men are reported. All had central scotomas of varying degrees, lowered visual acuity and round macular lesions. All had been looking through a "sunglass screen," which the author had not seen but assumed was inefficient. He believes that as a temporary expedient Crookes B2 lenses absorb enough infra-red rays to justify their use for protection but believes that standardized protective equipment should be devised and issued to the armed forces.

G M BRUCE

### Therapeutics

TISSUE THERAPY V P Filatov, *Vrach delo* 11 499, 1945

The basic method of tissue therapy is the transplantation of preserved tissue (skin of a living person or of the cadaver, placenta or other organs) for a period of six or seven days at a temperature of 2 to 4 C into the skin of the recipient. The sterilization of the preserved tissue in the autoclave at a temperature of 120 C does not deprive the tissue of its therapeutic action. Filatov therefore uses at present implantation (instead of transplantation) of tissue material into a skin pocket or under the conjunctiva. The material may be homogenous, autogenous or heterogenous.

The implantation may be repeated every two or three weeks. Filatov and his school also used subcutaneous injections of aqueous extracts of the preserved tissue. He also employed for the first time injections of extract of preserved leaves of aloe (kept in the dark for fifteen days), as in his opinion they contain biogenic stimulators. Cerebrospinal fluid from the cadaver, aqueous humour from cattle, cod liver oil and stored autoblood were also used. The technic of the preparation of the tissue, of aqueous extract and of the green leaves of plants is given in detail.

Tissue therapy gave excellent results with many diseases of the eye. Improvement of trachomatous pannus was observed in hundreds of cases as a result of injections of extracts and implantation of preserved, autoclaved material under the skin or the conjunctiva. Tissue therapy was also effective in the treatment of interstitial keratitis (of syphilitic origin) and tuberculous and herpetic keratitis. Recurrence and the acute symptoms were abolished with tissue therapy. In a number of cases of uveitis and opacities in the vitreous improvement followed tissue therapy. In cases of uveitis tissue therapy was frequently combined with autohemotherapy and specific treatment.

About 150 patients with retinitis pigmentosa were given tissue therapy. The visual acuity, the visual fields and dark adaptation (measured with the adaptometer) were increased to a striking degree. The night blindness disappeared in a few cases. The chorioretinitis of myopia responded to tissue therapy to a certain degree. In some cases there were increase of vision and decrease of central scotomas. The hemorrhages and opacities in the vitreous absorbed much faster than when no treatment was employed.

O SITCHEVSKA

# Society Transactions

EDITED BY DR W L BENEDICT

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NEW YORK ACADEMY OF MEDICINE, SECTION OF OPHTHALMOLOGY

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Feb 18, 1946

## Retrolental Fibroplasia in Premature Infants Terry's Syndrome

DR OLGA SITCHEVSKA (by invitation)

Terry (*Am J Ophth* 25 1409-1423, 1942) has given the following salient clinical characteristics of retrolental fibroplasia 1 The condition occurs in about 12 per cent of premature babies who weigh 3 pounds (1,360 Gm) or less 2 There is an opaque, vascularized membrane behind the lens, a growth of embryonic connective tissue 3 The anterior chambers are shallow or absent 4 The condition is bilateral 5 The color of the iris is "fetal blue" and changes slowly to muddy gray or brown 6 Thin ciliary processes can be seen in front of the opaque membrane 7 The eyes have a searching nystagmus 8 The eyes are usually small

Dr Terry has examined periodically about 100 babies with retrolental fibroplasia and knows of about 300 infants with the condition

Two cases were presented

Both babies were born prematurely, at the fetal age of 6½ months, and weighed less than 3 pounds In the case of the male infant the diagnosis of retinoblastoma was first made and later changed to retrolental fibroplasia Examination of the right eye showed posterior synechias, absence of the anterior chamber and increased tension, with no response to mydriatics The left eye had a shallow anterior chamber, and on dilatation a grayish, vascularized membrane could be seen above The child was about 2 years old at the time of the report, and his physical and mental development was normal The tension appeared normal in both eyes (without medication) The irises were of a "fetal blue" color, but the left eye was beginning to turn to a muddy brown The eyes were rather large

The female baby had very small eyes The right eye showed searching nystagmus and posterior synechias, the left eye dilated freely, and a gray membrane could be seen behind the lens, which thinned considerably during the period of observation At the time of the report the grayish membrane appeared like heavy opacities of the vitreous Intraocular tension had been normal

Neither baby had any light projection Both infants were seen by Dr Terry, who confirmed the diagnosis of retrolental fibroplasia

## DISCUSSION

DR RUTH MORRIS BAKWIN Retrolental fibroplasia is of great interest to the pediatrician To what extent this condition affects the mental development of the child is not known One of the patients presented by Dr Sitchevska had an intelligence quotient of 128, one of superior intelligence, on the interim Hayes-Binet test

In the past decade this condition has increased out of proportion to the rate of survival of premature infants. The mortality rate has remained at about the same level since 1933—25 to 26 per hundred thousand of the population.

Of the 150 patients reported by Dr. Reese and Dr. Terry, 95 were males and 55 females. If this ratio is borne out by other studies, it would seem that retrolental fibroplasia is sex linked.

### Construction of Lacrimal Passage: Report of a Case and Discussion of Experience with the Procedure. DR. LOREN P. GUY

The case of a Sicilian woman aged 26 for whom was constructed a new lacrimal passage is presented and illustrated with lantern slides. The surgical technic employed was similar to that presented to this society on Dec. 15, 1941, and published later (*Surgical Construction of a Lacrimal Passage*, ARCH. OPHTH. 29: 575-577 [April] 1943) except that a skin graft was used instead of a mucous membrane graft, since the latter was not readily available. The skin graft took well in spite of there being unexpected infection in the ethmoid cells, and the patient had a patent lacrimal passage at the time of the report, five months after the operation. This passage was about 75 per cent as efficient as a normal natural passage.

The patient had had five operations on the lacrimal passage, the first consisting in probing at the age of 4 months. The lacrimal sac had been removed, and there was a disfiguring scar over the area. Removal of this scar tissue has improved the appearance of the ocular region.

A lacrimal passage lined with skin epithelium will remain patent, but if mucous membrane is available it is the tissue of choice.

#### DISCUSSION

DR. OSCAR GREGOR: The use of an elastic hollow rubber catheter is an improvement in the surgical technic of replacement of a lacrimal passage. Royales, of Madrid, and Morax used nonelastic wax around which a graft was wrapped. The method was disappointing, to quote Dr. S. A. Gifford: "The Morax method of employing a Tiersch graft wound around a small peg is difficult and often unsuccessful." Apparently, the graft must be exposed to proper pressure, and the compressibility of the hollow rubber tube furnishes this. McWilliams (*Principles of the Four Types of Skin Grafting*, J. A. M. A. 83: 183 [July 19] 1924) stated: "Pressure is the keynote of success in using free grafts, being next to asepsis in importance."

Mucous membrane seems superior to skin as a source of a graft in this situation, as skin remains skin and exfoliation of the keratinized areas may endanger the free passage. However, the resistance that the skin in the case reported had to infection must be borne in mind, and the use of the skin graft must be reappraised in the light of future experience.

DR. HENRY E. BRANCA: The diagnosis of right-sided acute purulent ethmoiditis was made at the time of operation, for when the opening was made into the nose and some of the ethmoid cells were ruptured there was a free discharge of pus into the wound. I was asked to treat the nose after operation, but I was unable to institute therapy until the



rubber catheter was removed, on the sixth day. At that time an intranasal examination revealed free pus in the right nasal cavity with a similar, but less severe, condition on the left side. After the pus had been suctioned out and the nasal membranes shrunk, examination revealed in the region of the agger nasi a small prominence of grayish tissue, which probably represented the graft, the middle meatus presented mucopus. The patient had the symptoms and signs of acute ethmoiditis. We treated the patient daily with the Proetz displacement method and with the application of astringents to the middle meatus. It took about twelve days for the ethmoiditis to clear up, and we were fortunate in getting the graft to take. I should like to believe that the care of the sinus condition played a role in bringing about the "take" of the graft.

### **Retrolental Fibroplasia** DR ARLINGTON C KRAUSE, Chicago

A summary of 18 cases of congenital encephalo-ophthalmic dysplasia of unknown origin was given. The ocular disease was similar to, or identical with, the retrolental fibroplasia described by Terry.

This dysplasia was more commonly found in premature infants and in infants from a multiple birth. The common neurologic signs in many cases were mental retardation, microcephalus and hydrocephalus. Mental retardation was frequently evidenced when the child became several years old. Postmortem examinations in 2 cases revealed hypoplasia, hyperplasia and heterotopias of the cerebrum and cerebellum and internal hydrocephalus.

The ocular signs were loss of vision, ptosis, endophthalmos, microphthalmos, strabismus, retinal detachment, retrolental masses, retinal atrophy and gliosis, retinal dysplasia, coloboma of the choroid and optic nerve, recurrent hemorrhages in the retina and vitreous, anterior and posterior synechias, secondary glaucoma and cataract.

In the more severe form of the disease, the child died of intercurrent infection or was placed in an institution for the feeble-minded.

### DISCUSSION

DR ALGERNON B REESE: May I point out the features of Dr Krause's contribution about which I feel there might be some room for disagreement? Although I do not agree with him on some of the fundamental aspects of his concept, his work is a stepping-stone toward a better understanding of this most vexing problem.

As Dr Krause has pointed out, for one hundred years or more basically related lesions have been reported under various synonyms, such as co-called persistent tunica vasculosa lentis, congenital membrane behind the lens and congenital connective tissue in the vitreous. These lesions formerly were rare. At our hospital my colleagues and I saw about 1 case every two years. They were usually in full term infants and were frequently unilateral. In the past decade the frequency has increased a great deal. We now see from 6 to 12 cases a year or more, the condition is usually bilateral and is more frequent in premature infants. Because of this increased incidence a great deal of attention has been given to the subject of late. More recently, Terry has described the anomaly occurring in premature babies as retrolental

fibroplasia. He felt that the lesion was acquired and that it was different from the condition which had been seen rather infrequently in the past. Dr Frank Payne and I (Persistence and Hyperplasia of the Primary Vitreous, *Am J Ophth* 29: 1-24 [Jan] 1946) stated the belief that the abnormality in these erstwhile sporadic cases and that in the more recent cases occurring in premature babies were one and the same basic lesion and that it represented the congenital remains of an angio-blastic mesoderm composing the primary vitreous and occurring with or without hyperplasia. We concluded that the increased incidence was due to the lowered mortality of premature infants, but Dr Bakwin's comments this evening lead me to the belief that we may have been wrong in this assumption.

Is the ocular lesion which Dr Krause describes the same as that which Terry and Payne and I have described? I have seen Dr Krause's illustrations, and I feel confident that we are all speaking of the same condition. Terry, calling the lesion retrolental fibroplasia, concluded it was an acquired manifestation and explained it on this basis. Payne and I, designating the lesion as persistence and hyperplasia of the primary vitreous, expressed the belief that the lesion represented congenital remains and hyperplasia of tissue which should have disappeared. Dr Krause, calling the lesion congenital encephalo-ophthalmic dysplasia, believes it represents a faulty development of the neuroectoderm in that portion where it forms the retina as well as the brain.

First, Dr Krause claims that the ocular lesion is a primary dysplasia of the retina. However, it seems to me that he does not explain the almost constant appearance of fibrous tissue in the vitreous. I cannot conceive of this fibrous tissue being secondary to a retinal dysplasia. Payne and I demonstrated in this fibrous tissue of the vitreous the presence of cartilage, smooth muscle, fat, connective tissue and blood vessels—in other words, all the derivatives of the mesoderm. This being true, it would seem that the fibrous tissue must represent a primary lesion in the vitreous. The presence of the hyaloid artery is a fairly common occurrence in these cases, and I cannot see how this fits into the picture of the retinal dysplasias. Hemorrhage is a frequent occurrence, and I do not see how hemorrhage can stem from dysplasia.

In Dr Krause's first illustration he showed a microscopic section in which the retina extended rather far forward and he spoke of this as a hyperplasia. It seemed to me that this retina extended forward to some fibrous tissue which was back of the lens in the neighborhood of the equator.

The microscopic sections in which he showed that there was no evidence of fibrous tissue back of the lens I regard as inconclusive, because serial sections (or at least sections throughout the area of the lens) should be made to rule out the presence of this fibrous tissue. In order to identify this fibrous tissue clinically, it is sometimes necessary to stand on your head, so to speak, in order to obtain a view sufficiently far to the periphery to appreciate the presence of the tissue at the equator of the lens.

Second, Dr Krause says that mental retardation, resulting from dysplasia or agenesis of the brain, is a part of the picture. (Perhaps one should define "mental retardation" to avoid a misunderstanding

in terms ) Except for 4 cases of hydrocephalus, which I feel it would be misleading to include, there was evidence of mental retardation in only 5 (or 30 per cent) of his cases. This incidence is no higher than that in the series of cases of cataract associated with rubella. Moreover prematurity itself and cerebral anoxia (a condition figuring in a surprisingly large number of Dr Krause's cases) predispose to a higher than normal incidence of mental retardation. In 82 per cent of Dr Krause's cases the babies were premature. If the 2 cases of cerebral agenesis (diagnosis not supported by autopsy observations) are also included with the cases of mental retardation in his series, that category would comprise 7 cases (or 38 per cent). On the basis of his evidence, it is not necessary to postulate cerebral agenesis to explain the slower development of these children. I wrote letters inquiring about the mental development in all the accessible cases in the series. Dr Payne and I reported. I had 18 replies, and 16 stated that the child was normal, i. e., that it had developed at the same pace as any other child of the same age. Only 2 (or 11 per cent) of the 18 children were mentally retarded. I do not believe that Dr Krause's findings justify him in the assumption that mental retardation is a usual accompaniment of the ocular lesion we are discussing tonight.

Lastly, what evidence of cerebral dysplasia or agenesis do Dr Krause's cases show? Except for the cases of hydrocephalus, in some of which autopsies were performed, there was only 1 case in which a complete autopsy report is given, including microscopic observations. This was case 10, which I feel does not belong in this category because the eyes, in my opinion, do not show the lesion under discussion.

DR BRITAIN F. PAYNE. I have brought two or three slides to illustrate in the human embryo some features of the background of the anomaly which has been so beautifully described here. Some one should review the development of the human eye for us, so that we may appreciate these points. Dr Reese calls this anomaly a developmental abnormality of the primary vitreous. I am not sure that I understand exactly what he means by primary vitreous. My interpretation of primary vitreous is, or at least it was a few years ago, simply that of fibers extending from the surface ectoderm to the neural ectoderm, and these fibers are truly the anlagen of the vitreous body. The secondary and the tertiary vitreous body are formed by mesoderm which comes in through the cleft, but also is fixed at a base, which later is located on the flat part of the ciliary body. The first slide shows the primary optic vesicle with the surface ectoderm thickening to form the lens plate, which is to come off and contribute the invagination. The next slide shows the invagination to form the secondary optic vesicle, and the lens vesicle is detached from the surface ectoderm. The fibrils extending from it to the primitive retina are, as I understand it, the primary vitreous body. The next stage has to do with the ingrowth of the mesoderm, which goes to form the secondary and the tertiary vitreous. While this process is going on, the central retinal vessels come in through the nerve and extend up to the lens vesicle, as shown in the next section. One can see here the hyaloid system with the vessels surrounding the lens itself. If for some reason, a child were born at this age, it would weigh under 3 pounds, and the chances are that

in the organization of this central retinal system one would have the formation of a membrane which would correspond to the one described by Terry, unless one considers that the hyaloid artery is a part of the vitreous, I do not see how one can arrive at any definite conclusion about it. In other words, it would have to be a part of the vitreous body if we consider it as Dr Reese explained it, and not a part of the remnants of the hyaloid system.

DR BLANCHE JACKSON, Boston. My associates and I have been working on the animal aspect of the problem primarily and have tried to find something which would produce the condition of retrolental fibroplasia in animals. Warkany's work on vitamin A deficiency in the rat has been repeated in our laboratory, and we have verified his finding that in this species the offspring of vitamin A-deficient mothers may show a fibroplasia-like growth of mesenchyme in the vitreous.

DR ARLINGTON C KRAUSE, Chicago. I think the cause of the fibroplasia, or whatever the condition is, is the answer to our questions. There are many questions I should like to ask Dr Reese about the primary vitreous. Is it part of the retina or not? And its hyperplasia—would that fall in with a retinal dysplasia or not?

It is fortunate that Terry has focused interest on this disease and brought it to the attention once more. Many patients will have to be seen and the origin and outcome of their condition studied.

I regret that I cannot answer all of Dr Reese's questions. That would require reading my paper again. A large number of children with this condition do have something wrong with their neural ectoderm, whether it ends in mental retardation or leads to their being institutionalized, as have 4 of my series up to the present time, not for their eyes, but for their low mentality. If one includes the hydrocephalic and the microcephalic cases, as Dr Reese does not, the group in which there is some mental aberration becomes rather large. I have been wondering whether there are not three types of fibroplasia—the Boston, the Knickerbocker and the midwestern. There may be a particular form of the disease in the particular locality. In Chicago one sees many detached retinas. In Boston Terry apparently has many cases of persistent hyaloid artery, and Dr Reese frequently sees fibroplasia of the vitreous. If, in considering the cases of rubella, as Dr Reese has, and as I have recently done, one notes a change in what this disease does to the child in utero. Such a child is affected very early, and the disease produces certain anomalies of the eye, which are more than mere cataract. It also affects the body in general, as is generally recognized, and there are cases of rubella in which low tone deafness, defects of the interventricular septum and other disturbances, such as—I dislike to say it again—mental retardation and microencephaly, are produced.

I am very much in accord with Dr Reese that all cases of fibroplasia do not appear in premature infants and that the disease may be unilateral, the infant is born with the disease, actually or potentially—actually, in the sense that the disorder may appear at birth, or potentially, in that it may develop afterward because the seeds of the

disorder are there In the discussion on the paper by Dr Reese and Dr Payne, Ida Mann summarized fibrioplasia well in one sentence

These cases are all good examples of the general principle of the production of developmental anomalies through the arrest at a definite stage of intra- or extra-uterine life followed by aberrant growth

This is another reason that I have called the disease congenital ophthalmic dysplasia

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COLLEGE OF PHYSICIANS OF PHILADELPHIA, SECTION ON OPHTHALMOLOGY

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George F J Kelly, M D , *Clerk*

March 21, 1946

Vascular Disease Associated with Angioid Streaks of the Retina and Pseudoxanthoma Elasticum

This paper was published in the March 1946 issue of the ARCHIVES, page 241

DISCUSSION

DR FRANCIS HEED ADLER The thesis of this communication is well founded, i e , that angioid streaks of the retina, osteitis deformans, pseudoxanthoma elasticum and some forms of peripheral vascular disease are parts of the same clinical entity, which is not as yet completely elucidated

The pathology of the arteries is not entirely clear, as is evidenced by the fact that a number of pathologists to whom these sections were shown were somewhat puzzled by them The general consensus seems to have been that the disease process was confined to the elastic tissue of the arteries It seems strange that no one had previously made a study of the changes in the elastic tissue of the arteries associated with angioid streaks of the retina, although it was mentioned in the literature that such changes might be present

These observations tend to confirm the opinion that the underlying pathologic process of angioid streaks in the retina is a degeneration of the elastic tissue of Bruch's membrane

DR GEORGE F J KELLY I should like to ask Dr Scheie whether he had much to do with getting this section of artery After all, this artery was a little patulous After he removed the piece, was there enough collateral circulation to carry on? I mean to say, one can get sections of skin but a section of an artery is a bit unusual

DR FRANK B WALSH, Baltimore It is interesting that pseudoxanthoma elasticum was associated with angioid streaks in all the cases described How frequently have the authors seen angioid streaks in the absence of changes in the skin?

MAJOR HAROLD SCHEIE, Medical Corps, Army of the United States In answer to Dr Kelly, we took the biopsy specimen with little hesitation because the ulnar artery was completely occluded Microscopic evidence further justified taking the specimen by verifying the occlusion

The wall of the artery and the tissues surrounding the artery showed newly formed and anastomotic vessels as large as the very minute residual lumen of the ulnar artery. The presence of a residual lumen was even debatable. When the artery was examined several sections higher, what seemed to be residual lumen at the lower level had shifted to one side and looked like any of the anastomotic vessels. Furthermore, the patient being an extremely intelligent soldier, the situation was explained to him. He was told that he would derive no benefit from the procedure but that we were desirous of obtaining further information which might possibly be of aid to others in the future.

In answer to Dr. Adler's question, clinical disease of the peripheral vessels is not mentioned in the literature. Scholz did mention absence of the peripheral pulse in 1 patient, but apparently he considered it no further.

Several references to degeneration of elastic tissue in arterial walls were found as part of routine microscopic studies.

**Symptomatology of Subdural Hematomas in Infants and in Adults with Particular Reference to Ocular Signs: Observations on Pathogenesis of Subdural Hematoma.** DR. CLIFTON D. GOVAN and DR. FRANK B. WALSH, Baltimore

This paper will be published in a future issue of the ARCHIVES

## Book Reviews

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**Ophthalmia Neonatorum. The Problem After Thirty Years of Statutory Notification and Sixty Years of Credé Prophylaxis** Institute of Ophthalmology Monographs no 1 By Arnold Sorsby, M D, F R C S Price not given Pp 66 London Hamish Hamilton, Ltd, 1945

All children who suffer from ophthalmia neonatorum in the County of London are admitted to the hospital of the London County Council, of which Professor Sorsby is the ophthalmic surgeon. His experience is therefore unique, and a monograph on this subject from his pen is, of course, completely authoritative.

Since 1914 notification of a purulent discharge from the eyes of a newborn infant has been compulsory in England and Wales. This booklet is a study of the problem of ophthalmia neonatorum. It is composed largely of tables, charts and graphs, and is therefore difficult to review and well nigh impossible to abstract. Nevertheless, many of the conclusions reached by the author are worth recording here. His approach is sound. He admits that the rates recorded by the Registrar General, consistent though they be, are not an unquestionable indication of the incidence of ophthalmia neonatorum, and he remarks that notification is designed for the purpose of insuring early and adequate treatment, not that of collecting statistics. He finds, however, that the incidence of blindness in children has declined considerably but is not convinced that this is due alone to the concurrent decline in the incidence of ophthalmia neonatorum. He shrewdly points out that other ophthalmias, notably the phlyctenular and syphilitic types, have also become less frequent.

It is interesting to note the revolution in opinion where etiology of conjunctivitis in the newborn is concerned. Originally, of course, the term "ophthalmia neonatorum" was practically synonymous with "gonorrheal conjunctivitis". Now the advances in bacteriologic investigation and the emergence of blennorrhea as a clinical entity have negated, and very nearly reversed, this conception. For example, a table listed 37 cases of ophthalmia neonatorum reported in 1914, in 20 of which the disease was gonococcic in origin. In the same table, in 1935, 37 cases are again reported, in none of which gonorrhea was present. Professor Sorsby finds that the most frequent cause is the staphylococcus (35 per cent). He places the gonococcus next (25 per cent) and viruses next (10 per cent).

The role played by prophylaxis in the reduction of this disease is well discussed, and some interesting conclusions are drawn. The author finds no evidence that silver nitrate is superior to some of the organic silver preparations, and he states that it calls for more care in its use. He draws attention to the instability of this disinfectant and advocates that it be supplied in paraffin-lined yellow wax (beeswax) capsules or other suitable containers.

The discussion of changing methods of therapy and their increasing efficacy is, in the opinion of this reviewer, the most important contri-

bution of this work When sulfonamide therapy was introduced, it was approximately four times as effective in a given time as were the older, local, procedures Later, the advent of penicillin relegated all other methods of cure to the background, and indeed rendered them obsolete The author says "The reduction of the duration of treatment from weeks by the older methods to days by the sulphonamides is paralleled by the reduction of treatment from several days by the sulphonamides to as many hours by penicillin"

The method of use of penicillin is as follows

1 On admission a swab is taken for smear and culture, and the eye is irrigated with half-normal saline solutions at room temperature A drop of epinephrine hydrochloride (1:1,000) is instilled and a scraping taken from the palpebral conjunctiva for examination for inclusion bodies

2 Pus is wiped away, and 1 drop of penicillin in a concentration of 2,500 units per cubic centimeter is instilled

3 These instillations are repeated every five minutes until there is no discharge Generally, a half-hour's to three hours' treatment is all that is needed Pus is disregarded, and no irrigations are necessary

4 When there is no longer any discharge, penicillin is instilled at half-hour intervals In about six to twelve hours the eyes appear normal, but the penicillin is continued hourly for twelve hours and every two hours for twenty-four hours thereafter

The author closes by pointing out that the advocacy of Gibson, made nearly fifty years before Credé, that the disease in the mother should be eradicated before parturition, is still largely unachieved

This monograph has consigned to a deserved oblivion many of the older theories of ophthalmia neonatorum and has brought the subject completely up to date It should, of course, be studied by all ophthalmologists, but obstetricians, bacteriologists and public health officers will also find that it can be read with profit to themselves and their charges

G M BRUCE

**Journal of the History of Medicine and Allied Sciences** Volume 1, number 1 Subscription, \$7.50 in the United States, Canada and Latin America Pp 132 Quarterly New York Henry Schuman, January 1946

The field of our science is so wide, its relations with other activities and interests of mankind so numerous and important, that one might well paraphrase the classic sentence to read "*medicus sum, et humani nihil a me alienum puto*" The appearance of a quarterly on the history of medicine is significant as a contribution to present day culture and the store of knowledge No exposition of the *raison d'être* and purpose of this publication could have been more clear and instructive than that of the editor, George Rosen, in his timely and interesting prologue to the initial number of volume 1

The medical thought of the past is, indeed an important element in the training of the physician and his collaborators, professional and lay, especially in times like the present There is in the United States only one other publication in this field the *Bulletin of the History*



of *Medicine*, edited by Siegerist. The *Journal* will supplement, rather than compete with it, and it welcomes, as it now presents, contributions on such aspects of the subject as public health, nursing, pharmacy, veterinary medicine and dentistry, as well as biographies of outstanding workers in these fields and in the many arts and sciences that impinge on medicine.

The table of contents lists chapters on "Animal Substances in *Materia Medica*" (MacKinney), "Galenicals of Vesalius" (Singer), "Pharmacopoeias in World History" (Urdang), "Earliest Dentistry Wood-Cuts" (Proskauer), "Incubator and Taboo" (Ackerknecht), "Medical Education in 17th Century England" (Phyllis Allen), and biographic notes on William Blake and John Hunter (Jane Oppenheimer) and on Waterhouse, Harrison, and de Monserrate, author of the first anatomy in the Spanish language (Saunders and O'Malley). "Notes and Queries" (editor, Fisch) and "Book Reviews" deal with similar topics and personalities.

This is rich fare, indeed, and holds much of interest for those who have leisure and inclination to browse in the highways and byways (Gifford) of medicine. Many of the chapters are richly illustrated with woodcuts from old treatises and manuals. In this connection, it is a matter of regret that most of the reproductions are on too small a scale and are badly reproduced. The paper stock may in part be responsible for this shortcoming. While it is matt, free from glare, and so, very easy on the eyes it, unfortunately, allows the ink to spread so that not a few minor details are lost. This applies as well to the text of subtitles and explanatory notes, especially those in Latin or in German (Gothic) type, which would add so greatly to the pleasure of medicohistorical study if they were not practically illegible. If in future issues of the journal these illustrative woodcuts were reproduced on special (calendered?) paper and, if possible, on a larger scale, little would be lacking for full enjoyment of this artistically and culturally valuable publication.

PERCY FRIDENBERG

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## News and Notes

EDITED BY DR W L BENEDICT

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### GENERAL NEWS

**Alumni Meeting of New York Eye and Ear Infirmary**—The first alumni meeting of the New York Eye and Ear Infirmary since the war will be held at 9 a. m., Sept. 7, 1946, at the New York Eye and Ear Infirmary, to be followed by a dinner at the University Club the same evening.

Communications should be addressed to B. F. Payne, M.D., acting secretary-treasurer, New York Eye and Ear Infirmary, 218 Second Avenue, New York 3.

# Directory of Ophthalmologic Societies \*

## INTERNATIONAL

### INTERNATIONAL ASSOCIATION FOR PREVENTION OF BLINDNESS

President Dr P Bailliart, 66 Boulevard Saint-Michel, Paris, 6<sup>e</sup>, France  
Secretary-General Prof M Van Duyse, Université de Gand, Gand, Prov Ost-flandern, Belgium  
All correspondence should be addressed to the Secretariat, 66 Boulevard Saint-Michel, Paris, 6<sup>e</sup>, France

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Place Habana, Cuba Time February 1948

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Place Eye, Ear, Nose and Throat Hospital, Chengtu, Szechuan, China

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Secretary Dr F S Tsang, 221 Foochow Rd, Shanghai

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President Dr H T Pi, Peiping Union Medical College, Peiping  
Secretary Dr C K Lin, 180 Hsi-Lo-yen Chienmeng, Peiping  
Place Peiping Union Medical College, Peiping Time Last Friday of each month

\* Secretaries of societies are requested to furnish the information necessary to make this list complete and keep it up to date

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 All correspondence should be addressed to the Assistant Secretary

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 Place Rosario Time Last Saturday of every month, April to November All correspondence should be addressed to the President

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AND OTOLARYNGOLOGY

Chairman Dr Savage Zerfoss, 165-8th Ave N, Nashville 3, Tenn  
 Secretary Dr Alston Callahan, 908 S 20th St, Birmingham 5, Ala  
 Place Miami, Florida Time Nov 6, 1946

## SOUTHWESTERN ACADEMY OF EYE, EAR, NOSE AND THROAT

President Dr H L Brehmer, 221 W Central Ave, Albuquerque, N Mex  
 Secretary Dr A E Cruthrds, 1011 Professional Bldg, Phoenix, Ariz

## SOUTHWESTERN MICHIGAN TRIOLOGICAL SOCIETY

President Dr W M Dodge, 716 First National Bank Bldg, Battle Creek  
 Secretary-Treasurer Dr Kenneth Lowe, 25 W Michigan Ave, Battle Creek  
 Time Last Thursday of September, October, November, March, April and May

## WESTERN PENNSYLVANIA EYE, EAR, NOSE AND THROAT SOCIETY

President Dr J V Foster, State College  
 Secretary-Treasurer Dr J McClure Tyson, Deposit National Bank Bldg, Dubois

## STATE

## ARKANSAS STATE MEDICAL SOCIETY, EYE, EAR, NOSE AND THROAT SECTION

President Dr E C Moulton, 619 Garrison Ave, Fort Smith  
 Secretary Dr K W Cosgrove, 7 Urquhart Bldg, Little Rock

## COLORADO OPHTHALMOLOGICAL SOCIETY

President Dr George H Stine, 23 E Pikes Peak Ave, Colorado Springs  
 Secretary Dr J Leonard Swigert, 320 Republic Bldg, Denver  
 Place University Club, Denver Time 7 30 p m, thurd Saturday of each month,  
 October to May, inclusive

CONNECTICUT STATE MEDICAL SOCIETY, SECTION ON EYE, EAR,  
NOSE AND THROAT

President Dr Paul B MacCready, 442 Temple St, New Haven  
 Secretary-Treasurer Dr W H Turnley, 1 Atlantic St, Stamford, Conn

## EYE, EAR, NOSE AND THROAT CLUB OF GEORGIA

President Dr William O Martin Jr, Doctors Bldg, Atlanta  
 Secretary-Treasurer Dr C K McLaughlin 666 Cherry St, Macon

## INDIANA ACADEMY OF OPHTHALMOLOGY AND OTO-LARYNGOLOGY

President Dr W E Stewart, 721 Wabash Ave, Terre Haute  
 Secretary Dr Russell A Sage, 23 E Ohio St, Indianapolis  
 Place French Lick Time First Wednesday in April

## IOWA ACADEMY OF OPHTHALMOLOGY AND OTO-LARYNGOLOGY

President Dr S A O'Brien, 1 N Federal Ave, Mason City

KANSAS STATE MEDICAL SOCIETY, SECTION ON OPHTHALMOLOGY AND  
OTOLARYNGOLOGY

President Dr W B Granger, Emporia  
 Secretary Dr George F Gsell, 911 Beacon Bldg, Wichita 2

LOUISIANA-MISSISSIPPI OPHTHALMOLOGICAL AND OTOLARYNGOLOGICAL SOCIETY

President Dr George S Adkins, 121 N President St, Jackson, Miss  
Secretary-Treasurer Dr Edley H Jones, 1301 Washington St, Vicksburg, Miss

MEDICAL SOCIETY OF THE STATE OF PENNSYLVANIA, SECTION ON  
EYE, EAR, NOSE AND THROAT DISEASES

Chairman Dr William T Hunt Jr, 1205 Spruce St, Philadelphia 7  
Secretary Dr Gabriel Tucker, 250 S 18th St, Philadelphia 3

MICHIGAN STATE MEDICAL SOCIETY, SECTION OF OPHTHALMOLOGY  
AND OTOLARYNGOLOGY

Chairman Dr Edmond L Cooper, 1553 Woodward Ave, Detroit 26  
Secretary Dr Ralph H Gilbert, 110 Fulton St E, Grand Rapids

MINNESOTA ACADEMY OF OPHTHALMOLOGY AND OTOLARYNGOLOGY

President Dr Karl C Wold, 1051 Lowry Bldg, St Paul 2  
Secretary Dr William A Kennedy, 372 St Peter St, St Paul 2  
Time Second Friday of each month from October to May

MONTANA ACADEMY OF OTO-OPHTHALMOLOGY

President Dr H Casebeer, 44 W Park Ave, Butte  
Secretary Dr Fritz D Hurd, 309 Medical Arts Bldg, Great Falls

NEBRASKA ACADEMY OF OPHTHALMOLOGY AND OTOLARYNGOLOGY

President Dr W Howard Morrison, 1500 Medical Arts Bldg, Omaha  
Secretary-Treasurer Dr John Peterson, 1307 N St, Lincoln

NEW JERSEY STATE MEDICAL SOCIETY, SECTION ON OPHTHALMOLOGY,  
OTOLOGY AND RHINOLARYNGOLOGY

Chairman Dr C W Buvinger, 50 Washington St, East Orange  
Secretary Dr Z Laurence Griesemer, 1145 E Jersey St, Elizabeth

NEW YORK STATE MEDICAL SOCIETY, EYE, EAR, NOSE AND  
THROAT SECTION

Chairman Dr Maxwell D Ryan, 660 Madison Ave, New York 21  
Secretary Dr Thomas H Johnson, 30 W 59th St, New York

NORTH CAROLINA EYE, EAR, NOSE AND THROAT SOCIETY

President Dr A J Ellington, 412 S Spring St, Burlington  
Secretary Dr J A Harrill, Bowman Gray School of Medicine, Winston-Salem  
Place Hendersonville Time Sept 16-19, 1946

NORTH DAKOTA ACADEMY OF OPHTHALMOLOGY AND OTO-LARYNGOLOGY

President Dr E D Perrin, 221-5th St, Bismarck  
Secretary-Treasurer Dr M T Lampert, Minot

OREGON ACADEMY OF OPHTHALMOLOGY AND OTO-LARYNGOLOGY

President Dr Wilfred Belnap, 833 S W 11th Ave, Portland  
Secretary-Treasurer Dr C W Kuhn, 1020 S W Taylor St, Portland 5  
Place Good Samaritan Hospital, Portland Time Third Tuesday of each month

PENNSYLVANIA ACADEMY OF OPHTHALMOLOGY AND OTOLARYNGOLOGY

President Dr Thomas F Furlong Jr, 36 Parking Plaza, Ardmore  
Secretary Dr Benjamin F Souders, 143 N 6th St, Reading  
Time Last week in April



## RHODE ISLAND OPHTHALMOLOGICAL AND OTOLOGICAL SOCIETY

Acting President Dr N Darrell Harvey, 112 Waterman St, Providence  
 Secretary-Treasurer Dr Linley C Happ, 124 Waterman St, Providence  
 Place Rhode Island Medical Society, Library, Providence Time 8 30 p m,  
 second Thursday in October, December, February and April

## SOUTH CAROLINA SOCIETY OF OPHTHALMOLOGY AND OTOLARYNGOLOGY

President Dr J H Stokes, 125 W Cheves St, Florence  
 Secretary-Treasurer Dr Roderick Macdonald, 330 E Main St, Rock Hill  
 Place Hendersonville, N C Time Sept 16-19, 1946

## TENNESSEE ACADEMY OF OPHTHALMOLOGY AND OTOLARYNGOLOGY

President Dr George Burchfield, Maryville  
 Secretary-Treasurer Dr Sam H Sanders, 1089 Madison Ave, Memphis

## TEXAS OPHTHALMOLOGICAL AND OTO-LARYNGOLOGICAL SOCIETY

President Dr F H Rosebrough, 603 Navarro St, San Antonio  
 Secretary Dr M K. McCullough, 1717 Pacific Ave, Dallas

## UTAH OPHTHALMOLOGICAL SOCIETY

President Dr E B Fairbanks, 315 Medical Arts Bldg, Salt Lake City  
 Secretary-Treasurer Dr Dean Spear, 516 Boston Bldg, Salt Lake City  
 Place University Club, Salt Lake City Time 7 00 p m, third Monday of  
 each month

## VIRGINIA SOCIETY OF OTO-LARYNGOLOGY AND OPHTHALMOLOGY

President Dr Thomas E Hughes, 1000 W Grace St, Richmond  
 Secretary-Treasurer Dr Francis H McGovern, 105 S Union St, Danville

WEST VIRGINIA STATE MEDICAL ASSOCIATION, EYE, EAR, NOSE AND  
THROAT SECTION

President Dr George Traugh, 309 Cleveland Ave, Fairmont  
 Secretary Dr Welch England, 621½ Market St, Parkersburg

## LOCAL

## AKRON ACADEMY OF OPHTHALMOLOGY AND OTOLARYNGOLOGY

President Dr E L Mather, 39 S Main St, Akron, Ohio  
 Secretary-Treasurer Dr V C Malloy, 2d National Bank Bldg, Akron, Ohio  
 Time First Monday in January, March, May and November

## ATLANTA EYE, EAR, NOSE AND THROAT SOCIETY

President Dr B M Cline, 153 Peachtree St N E, Atlanta, Ga  
 Secretary Dr Lester A Brown, 815 Doctors Bldg, Atlanta, Ga  
 Place Academy of Medicine Time 7 30 p m, fourth Monday of each month  
 from October to May

## BALTIMORE MEDICAL SOCIETY, SECTION ON OPHTHALMOLOGY

Chairman Dr Jonas Friedenwald, 1212 Eutaw Pl, Baltimore  
 Secretary Dr Fred Reese, 330 N Charles St, Baltimore 1  
 Place Medical and Chirurgical Faculty, 1211 Cathedral St Time 8 30 p m,  
 fourth Thursday of each month from October to March

BIRMINGHAM EYE, EAR, NOSE AND THROAT CLUB

President Each member, in alphabetical order  
 Secretary Dr W Chunn Parsons, 425 Woodward Bldg, Birmingham, Ala  
 Place Tutwiler Hotel Time 6 30 p m, second Tuesday of each month, September to May, inclusive

BROOKLYN OPHTHALMOLOGICAL SOCIETY

President Dr Benjamin C Rosenthal, 140 New York Ave, Brooklyn  
 Secretary-Treasurer Dr Louis Freemark, 256 Rochester Ave, Brooklyn 13  
 Place Kings County Medical Society Bldg, 1313 Bedford Ave Time Third Thursday in February, April, May, October and December

BUFFALO OPHTHALMOLOGIC CLUB

President Dr William M Howard, 389 Linwood Ave, Buffalo 9  
 Secretary-Treasurer Dr Sheldon B Freeman, 196 Linwood Ave, Buffalo 9  
 Time Second Thursday of each month from October to May

CHATTANOOGA SOCIETY OF OPHTHALMOLOGY AND OTOLARYNGOLOGY

President Each member, in alphabetical order  
 Secretary Dr Douglas Chamberlain, Providence Bldg, Chattanooga, Tenn  
 Place Mountain City Club Time Second Thursday of each month from September to May

CHICAGO OPHTHALMOLOGICAL SOCIETY

President Dr W A. Mann, 30 N Michigan Ave, Chicago 2  
 Secretary Dr J. R Fitzgerald, 3215 W North Ave, Chicago  
 Place Continental Hotel, 505 N Michigan Ave Time Third Monday of each month from October to May

CINCINNATI GENERAL HOSPITAL OPHTHALMOLOGY STAFF

Chairman Dr D T Vail, 441 Vine St, Cincinnati  
 Secretary Dr A A Levin, 441 Vine St, Cincinnati  
 Place Cincinnati General Hospital Time 7 45 p m, third Friday of each month except June, July and August

CLEVELAND OPHTHALMOLOGICAL CLUB

Chairman Dr M Paul Motto, Rose Bldg, Cleveland  
 Secretary Dr H H Wygand, 624 Guardian Bldg, Cleveland  
 Time Second Tuesday in October, December, February and April

COLLEGE OF PHYSICIANS, PHILADELPHIA, SECTION ON OPHTHALMOLOGY

Chairman Dr Burton Chance, 317 S 15th St, Philadelphia  
 Clerk Dr George F J Kelly, 37 S 20th St, Philadelphia  
 Time Third Thursday of every month from October to April, inclusive

COLUMBUS OPHTHALMOLOGICAL AND OTO-LARYNGOLOGICAL SOCIETY

Chairman Dr M Goldberg, 328 E State St, Columbus, Ohio  
 Secretary-Treasurer Dr W J Miller, 21 E State St, Columbus, Ohio  
 Place University Club Time 6 15 p m, first Monday of each month, from October to May, inclusive

CORPUS CHRISTI EYE, EAR, NOSE AND THROAT SOCIETY

Chairman Dr L W O Janssen, 710 Medical Professional Bldg, Corpus Christi, Texas  
 Secretary Dr F B Kelly, 519 Medical Professional Bldg, Corpus Christi, Texas  
 Time 6 30 p m, third Tuesday of each month from October to May

## DALLAS ACADEMY OF OPHTHALMOLOGY AND OTO-LARYNGOLOGY

President Dr Speight Jenkins, 1719 Pacific Ave, Dallas, Texas  
 Secretary Dr L Darrough, Dallas Medical and Surgical Clinics, Dallas, Texas  
 Place Dallas Athletic Club Time 6 30 p m, first Tuesday of each month  
 from October to June The November, January and March meetings are  
 devoted to clinical work

## DES MOINES ACADEMY OF OPHTHALMOLOGY AND OTOLARYNGOLOGY

President Dr H I McPherrin, 406-6th Ave, Des Moines, Iowa  
 Secretary-Treasurer Dr C C Jones, Bankers Trust Bldg, Des Moines, Iowa  
 Time 7 45 p m, fourth Monday of every month from September to May

## DETROIT OPHTHALMOLOGICAL CLUB

Chairman Members rotate alphabetically  
 Secretary Dr Wesley G Reid, 974 Fisher Bldg, Detroit 2  
 Place Club rooms of Wayne County Medical Society Time First Monday of  
 each month, November to April, inclusive

## DETROIT OPHTHALMOLOGICAL SOCIETY

President Dr Bruce Frahck, 201 S Main St, Ann Arbor, Mich  
 Secretary Dr William S Gonne, 619 David Whitney Bldg, Detroit 26  
 Place Club rooms of Wayne County Medical Society Time 6 30 p m, third  
 Thursday of each month from November to April, inclusive

## EASTERN NEW YORK EYE, EAR, NOSE AND THROAT ASSOCIATION

President Dr Frank C Furlong, 713 Union St, Schenectady  
 Secretary-Treasurer Dr E Martin Freund, 762 Madison Ave, Albany  
 Time Third Wednesday in October, November, March, April, May and June

## FORT WORTH EYE, EAR, NOSE AND THROAT SOCIETY

President Dr C R Lees, 602 W 16th St, Fort Worth 2, Texas  
 Secretary-Treasurer Dr Van D Rathgeber, 1305 Medical Arts Bldg, Fort  
 Worth, Texas  
 Place Medical Hall, Medical Arts Bldg Time 7 30 p m, first Friday of each  
 month except July and August

HOUSTON ACADEMY OF MEDICINE, OPHTHALMOLOGICAL AND  
OTO-LARYNGOLOGICAL SECTION

President Dr J Matt Robison, 1304 Walker Ave, Houston, Texas  
 Secretary Dr John H Barrett, 1304 Walker Ave, Houston, Texas  
 Place River Oaks Country Club Time 6 30 p m, second Thursday of each  
 month from October to June

## INDIANAPOLIS OPHTHALMOLOGICAL AND OTOLARYNGOLOGICAL SOCIETY

President Dr J Jerome Littell, 603 Hume Mansur Bldg, Indianapolis  
 Secretary Dr J Lawrence Sims, 23 E Ohio St, Indianapolis  
 Place Indianapolis Athletic Club Time 6 30 p m, second Thursday of each  
 month from November to May

## KANSAS CITY SOCIETY OF OPHTHALMOLOGY AND OTO-LARYNGOLOGY

President Dr Edgar Johnson, 906 Grand Ave, Kansas City, Mo  
 Secretary Dr W E Keith, 1103 Grand Ave, Kansas City, Mo  
 Time Third Thursday of each month from October to June The November,  
 January and March meetings are devoted to clinical work.

LONG BEACH EYE, EAR, NOSE AND THROAT SOCIETY

Chairman Dr Francis Carl Hertzog, 117 E 8th St, Long Beach, Calif  
 Secretary-Treasurer Dr Robert G Thornburgh, 117 E 8th St, Long Beach, Calif  
 Place Seaside Hospital Time Last Wednesday of each month from October to May

LOS ANGELES SOCIETY OF OPHTHALMOLOGY AND OTOLARYNGOLOGY

President Dr A R Robbins, 1930 Wilshire Blvd, Los Angeles  
 Secretary-Treasurer Dr K C Brandenburg, 110 Pine Ave, Long Beach 2, Calif  
 Place Los Angeles County Medical Association Bldg, 1925 Wilshire Blvd Time  
 6 30 p m, fourth Monday of each month from September to May, inclusive

LOUISVILLE EYE AND EAR SOCIETY

President Dr Joseph S Heitger, Heyburn Bldg, Louisville, Ky  
 Secretary-Treasurer Dr J W Fish, 321 W Broadway, Louisville, Ky  
 Place Brown Hotel Time 6 30 p m, second Thursday of each month from September to May, inclusive

LOWER ANTHRACITE EYE, EAR, NOSE AND THROAT SOCIETY

Chairman Each member in alphabetical order  
 Secretary Dr James J Monohan, 31 S Jardin St, Shenandoah, Pa

MEDICAL SOCIETY OF THE DISTRICT OF COLUMBIA, SECTION OF  
 OPHTHALMOLOGY AND OTOLARYNGOLOGY

Chairman Dr P S Constantinople, 1835 I St N W, Washington  
 Secretary Dr Frazier Williams, 1801 I St N W, Washington  
 Place 1718 M St N W Time 8 p m, third Friday of each month from October to April, inclusive

MEMPHIS SOCIETY OF OPHTHALMOLOGY AND OTOLARYNGOLOGY

Chairman Each member, in alphabetical order  
 Secretary Dr Sam H Sanders, 1089 Madison Ave, Memphis, Tenn  
 Place Eye Clinic of Memphis Eye, Ear, Nose and Throat Hospital Time 8 p m,  
 second Tuesday of each month from September to May

MILWAUKEE OTO-OPHTHALMIC SOCIETY

President Dr Ralph T Rank, 238 W Wisconsin Ave, Milwaukee  
 Secretary-Treasurer Dr Frank G Treskow, 411 E Mason St, Milwaukee 2  
 Place University Club Time 6 30 p m, fourth Tuesday of each month from October to May

MONTGOMERY COUNTY MEDICAL SOCIETY

Chairman Dr H V Dutrow, 1040 Fidelity Medical Bldg, Dayton, Ohio  
 Secretary-Treasurer Dr Maitland D Place, 981 Reibold Bldg, Dayton, Ohio  
 Place Van Cleve Hotel Time 6 30 p m, first Tuesday of each month from October to June, inclusive

MONTREAL OPHTHALMOLOGICAL SOCIETY

President Dr J Rosenbaum, 1396 Ste Catherine St W, Montreal Canada  
 Secretary Dr L Tessier, 1230 St Joseph Blvd E, Montreal, Canada  
 Time Second Thursday of October, December, February and April

NASHVILLE ACADEMY OF OPHTHALMOLOGY AND OTOLARYNGOLOGY

Chairman Dr M M Cullom, 700 Church St, Nashville, Tenn  
 Secretary Dr R E Sullivan, 432 Doctors Bldg, Nashville 3, Tenn  
 Place James Robertson Hotel Time 6 30 p m, third Monday of each month from October to May

## NEW ORLEANS OPHTHALMOLOGICAL AND OTOLARYNGOLOGICAL SOCIETY

President Dr W B Clark, 1012 American Bank Bldg, New Orleans  
 Secretary Dr Mercer G Lynch, 1018 Maison Blanche Bldg, New Orleans  
 Place Louisiana State University Medical Bldg Time 8 p m, second Tuesday  
 of each month from October to May

## NEW YORK ACADEMY OF MEDICINE, SECTION OF OPHTHALMOLOGY

Chairman Dr Brittain F Payne, 17 E 72d St, New York 21  
 Secretary Dr Milton Berliner, 57 W 57th St, New York  
 Time 8 30 p m, third Monday of every month from October to May, inclusive

## NEW YORK SOCIETY FOR CLINICAL OPHTHALMOLOGY

President Dr Benjamin Friedman, 6 W 77th St, New York  
 Secretary Dr Benjamin Esterman, 983 Park Ave, New York 28  
 Place New York Academy of Medicine, 2 E 103d St Time 8 p m, first Monday  
 of each month from October to May, inclusive

## OKLAHOMA CITY ACADEMY OF OPHTHALMOLOGY AND OTOLARYNGOLOGY

President Dr S R Shaver, 117 N Broadway, Oklahoma City  
 Secretary Dr William Mussil, Medical Arts Bldg, Oklahoma City  
 Place University Hospital Time Second Tuesday of each month from Sep-  
 tember to May

OMAHA AND COUNCIL BLUFFS OPHTHALMOLOGICAL AND  
OTO-LARYNGOLOGICAL SOCIETY

President Dr A A Stemberg, 1502 Farnam St, Omaha  
 Secretary-Treasurer Dr W Howard Morrison, 1500 Medical Arts Bldg, Omaha 2  
 Place Omaha Club, 20th and Douglas Sts, Omaha Time 6 p m dinner, 7 p m  
 program, third Wednesday of each month from October to May

## PASSAIC-BERGEN OPHTHALMOLOGICAL CLUB

President Dr Thomas Sanfacon, 340 Park Ave, Paterson, N J  
 Secretary-Treasurer Dr J Averbach, 435 Clifton Ave, Clifton, N J  
 Place Paterson Eye and Ear Infirmary Time 9 p m, last Friday of every  
 month, except June, July and August

## PHILADELPHIA COUNTY MEDICAL SOCIETY, EYE SECTION

President Dr L Waller Winckler, Philadelphia  
 Secretary Dr Robert T M Donnelly, 255 S 17th St, Philadelphia  
 Time First Thursday of each month from October to May

## PITTSBURGH OPHTHALMOLOGICAL SOCIETY

President Dr Jav G Linn, Jenkins Arcade, Pittsburgh  
 Secretary Dr Robert J Billings, Jenkins Arcade, Pittsburgh  
 Place Pittsburgh Academy of Medicine Bldg Time Fourth Monday of each  
 month, except June, July, August and September

## READING EYE, EAR, NOSE AND THROAT SOCIETY

President Dr Claude W Bankes, 212 N 6th St, Reading, Pa  
 Secretary Dr Paul C Craig, 232 N 5th St, Reading, Pa  
 Place Wyomissing Club Time 6 30 p m, third Wednesday of each month  
 from September to July

RICHMOND EYE, EAR, NOSE AND THROAT SOCIETY

President Dr Luther C Brawner, Professional Bldg, Richmond, Va  
 Secretary Dr Clifford A Folkes, Professional Bldg, Richmond, Va  
 Place Westmoreland Club Time 6 p m, second Monday of each month from  
 October to May

ROCHESTER EYE, EAR, NOSE AND THROAT SOCIETY

President Dr Frank Barber, 75 S Fitzhugh St, Rochester, N Y  
 Secretary-Treasurer Dr Charles T Sullivan, 277 Alexander St, Rochester, N Y

ST LOUIS OPHTHALMIC SOCIETY

President Dr A Lange, 3903a Olive St, St Louis  
 Secretary Dr William Kleinberg, Frisco Bldg, St Louis  
 Place Oscar Johnson Institute Time Fourth Friday of each month from October  
 to April, inclusive, except December, at 8 00 p m

SAN ANTONIO OPHTHALMO-OTO-LARYNGOLOGICAL SOCIETY

President Dr Belvin Pritchett, 705 E Houston St, San Antonio 5, Texas  
 Secretary-Treasurer Lt Col John L Matthews, AAF School of Aviation Medi-  
 cine, Randolph Field, Texas  
 Place San Antonio, Brooke General Hospital, Randolph Field or San Antonio  
 Aviation Cadet Center Time 7 p m, second Tuesday of each month from  
 October to May

SAN FRANCISCO COUNTY MEDICAL SOCIETY, SECTION ON EYE,  
 EAR, NOSE AND THROAT

Chairman Dr C B Cowan, 490 Post St, San Francisco  
 Secretary Dr D Harrington, 384 Post St, San Francisco  
 Place Society's Bldg, 2180 Washington St, San Francisco. Time Fourth  
 Tuesday of every month except June, July and December

SHREVEPORT EYE, EAR, NOSE AND THROAT SOCIETY

President Dr David C Swearingen, Slattery Bldg, Shreveport, La  
 Secretary-Treasurer Dr Kenneth Jones, Medical Arts Bldg, Shreveport, La  
 Place Shreveport Charity Hospital Time 7 30 p m, first Monday of every  
 month except July, August and September

SPOKANE ACADEMY OF OPHTHALMOLOGY AND OTO-LARYNGOLOGY

President Dr Robert L Pohl, W 1104, 21st Ave, Spokane, Wash  
 Secretary Dr Malcolm N Wilmes, 407 Riverside Ave, Spokane, Wash  
 Place Spokane Medical Library Time 8 p m, fourth Tuesday of each month  
 except June, July and August

SYRACUSE EYE, EAR, NOSE AND THROAT SOCIETY

President Dr A H Rubenstein, 713 E Genesee St, Syracuse, N Y  
 Secretary-Treasurer Dr I H Blaisdell, 713 E Genesee St, Syracuse, N Y  
 Place University Club Time First Tuesday of each month except June, July  
 and August

TOLEDO EYE, EAR, NOSE AND THROAT SOCIETY

Chairman Dr W W Randolph, 1838 Parkwood Ave, Toledo 2, Ohio  
 Secretary Dr John L Roberts, 316 Michigan St, Toledo, Ohio  
 Place Toledo Club Time Each month except June, July and August

## TORONTO ACADEMY OF MEDICINE, SECTION OF OPHTHALMOLOGY

Chairman Dr R G C Kelly, 14 Lynwood Ave, Toronto 5, Canada

Secretary Dr Alfred J Elliot, 802 Medical Arts Bldg, Toronto 5, Canada

Place Academy of Medicine, 13 Queens Park Time First Monday of each month, November to April

## WASHINGTON, D C, OPHTHALMOLOGICAL SOCIETY

President Dr Harold M Downey, 1740 M St N W, Washington, D C

Secretary-Treasurer Dr Richard W Wilkinson, 1408 L St N W, Washington, D C

Place Medical Society of District of Columbia Bldg, 1718 M St N W, Washington, D C Time 7 30 p m, first Monday in November, January, March and May

## WILKES-BARRE OPHTHALMOLOGICAL SOCIETY

Chairman Each member in turn

Secretary Dr Samuel T Buckman, 70 S Franklin St, Wilkes-Barre, Pa

Place Office of chairman Time Last Tuesday of each month from October to May

## CONGENITAL ENCEPHALO-OPHTHALMIC DYSPLASIA

ARLINGTON C KRAUSE, M D

CHICAGO

**P**RENATAL and neonatal retinopathy with congenital cerebral dysplasia is a rare syndrome. It is believed that the term "congenital encephalo-ophthalmic dysplasia" would be a suitable name for this disease, since chiefly the brain and the retina with their associated structures (but not the spinal cord) are affected by the disease, which has its origin in prenatal life. Parts of the syndrome occurring in a few cases have been described previously, but the disease has not been studied as a general pathologic process and a clinical entity. Various aspects have been presented—the ocular disease by the ophthalmologists, the cerebral dysplasia and hydrocephalus by the neurologists and the blindness and mental retardation by psychologists and psychiatrists.

The disease is characterized by retinal and cerebral hypoplasia and hyperplasia. The ocular disease is made manifest by the secondary changes, these include microphthalmos, malformations of the retina, choroid and optic nerve, retinal dysplasia, retinal glial membranes, cones and septums, and persistent remains of the hyaloid artery. Retinal detachment is associated with the same process which causes retinal dysplasia. The secondary effects are retinal atrophy, gliosis, fibrosis, intraocular hemorrhages and exudates, secondary glaucoma, atrophy of the iris, anterior and posterior synechias, cyclitic membranes, choroidal and scleral atrophy and cataracts.

The cerebral dysplasia is shown by the heterotopias and the hyperplasia, hypoplasia and aplasia of the cerebrum and the cerebellum. The secondary effects are the hydrocephalus, arising from the cerebral and arachnoidal dysplasia, and the microcephaly, reflected from the microencephaly resulting from the cerebral and cerebellar agenesis.

The syndrome is sometimes cryptic and is not always complete. The signs of the disease may be hidden at birth. The ocular disease may become evident later, but only on close examination. Clinically, the

From the Division of Ophthalmology, Department of Surgery, University of Chicago

Presented at a meeting of the New York Academy of Medicine, Section of Ophthalmology, Feb 18, 1946. A discussion of this paper appears in the September 1946 issue of the ARCHIVES, page 326.



ocular symptoms are usually easily discovered several months after birth, but the cerebral signs are not so evident unless the child has definite cerebral agenesis or hydrocephalus or later shows pronounced mental retardation not related to loss of vision. Apparently, the mildest forms of the ocular disease may occur as a small area of retinal atrophy or as a slight structural anomaly of the eye, the mildest cerebral disease may be an unrecognizable, slight cerebral dysplasia. Clinically, the disease may affect only the eye, or perhaps only the brain. One part of the syndrome may be observed clinically, and the other part may be discovered at autopsy. In the severe form of the disease the infant may have early fetal hydrocephalus and detached, dystrophic retinas and may die in utero.

### HISTORICAL SURVEY

*Retrolental Fibroplasia*—The 18 cases of congenital encephalo-ophthalmic dysplasia in this study are similar to or identical with Terry's cases reported under the title of fibroplasia.<sup>1</sup> The best definition of the term was given in 1944,<sup>1e</sup> when he stated

The development of embryonic connective tissue in the meshwork of the persistent hyaloid artery system behind the crystalline lens as a result of improper development of the inner eye, usually developing 3 to 5 months after birth in the extremely premature infant, is a disease entity which I call "retrolental fibroplasia."

Terry's first 6 cases<sup>1b</sup> were those of infants from 6 to 7 months of age with symptoms of blindness, nystagmoid movements and squint, noticed four to six months after birth. The children were born prematurely after twenty-seven to thirty-six weeks' gestation, with weights at birth of from 907 to 1,673 Gm. The eyes showed nystagmoid movements, a shallow anterior chamber and a gray pupillary reflex due to a retrolental mass, which presumably was derived from mesodermal tissue. Both eyes were involved in all cases. In 1 eye a small area of chorioretinal atrophy was observed. In another eye the gray reflex, or membrane, was incomplete nasally, so that the fundus was seen.

In 2 cases there were posterior synechias, and in 3 cases the pupils reacted to light. In 3 cases the eyes were small, and in 2 cases a

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1 Terry, T. L. (a) Extreme Prematurity and Fibroblastic Overgrowth of Persistent Vascular Sheath Behind Each Crystalline Lens, *Am J Ophth* **25** 203, 1943, (b) Fibroblastic Overgrowth of Persistent Tunica Vasculosa Lentis in Premature Infants. II Report of Cases, Clinical Aspects, *Arch Ophth* **29** 36 (Jan) 1943, (c) IV Etiologic Factors, *ibid* **29** 54 (Jan) 1943, (d) Fibroblastic Overgrowth of Persistent Tunica Vasculosa Lentis in Infants Born Prematurely. III Studies in Development and Regression of Hyaloid Artery and Tunica Vasculosa Lentis, *Am J Ophth* **25** 1409, 1942, (e) Retrolental Fibroplasia, *Proc Inst Med Chicago* **15** 150, 1944, (f) Retrolental Fibroplasia in Premature Infants. V Further Studies on Fibroblastic Overgrowth of Persistent Tunica Vasculosa Lentis, *Arch Ophth* **33** 203 (March) 1945.

hyaloid artery was seen. The seventh, or last, case was that of an infant born only twenty-six days prematurely and weighing 3,421 Gm at birth. One eye was removed on the basis of a diagnosis of probable retinoblastoma. No hyaloid artery or retiolental fibroplasia was found on pathologic examination. A large cone of glial tissue projected forward from the optic nerve. A few filaments of tissue connected the tip of the cone with the lens and the ora seriata. Later, Terry<sup>11</sup> omitted the seventh case from this series because the same disease occurred in another child in the family.

*Persistent Hyaloid Artery and Fibroplasia*—The question arises whether or not this so-called retiolental fibroplasia is comparable to other cases in the literature in which fibrous tissue was associated with a persistent hyaloid artery. A review of 31 cases<sup>2</sup> collected from the

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literature in which a clinical diagnosis of persistent hyaloid artery had been made revealed the following grouping (1) 1 case of metastatic ophthalmitis, which may be discarded, (2) 2 clinical cases without post-lental fibrous tissue, in 1 of which a persistent hyaloid artery only was seen and in the other a network of vessels lay on the posterior capsule, (3) 2 clinical cases in which a white reflex was seen unilaterally, (4) 3 clinical cases with a posterior polar cataract and a hyaloid artery, (5) 3 clinical cases with a gray mass in the pupil, which on removal showed retrolental fibrous tissue but no hyaloid artery, and (6) 20 cases with a gray pupillary reflex, retrolental fibrous tissue and a persistent hyaloid artery

The 26 cases of the last three groups may be classified under retrolental fibroplasia with a persistent hyaloid artery and are taken for analysis. The symptoms were blindness, nystagmoid movements and a white pupillary reflex. Prematurity was not mentioned. It is remarkable that in every case the lesion was unilateral. The anterior chamber was observed to be shallow in 11 cases, and posterior synechias were present in 10 cases. In 16 cases the symptoms pertaining to the abnormal eye were noticed before the age of 6 months. In 20 cases a pre-operative diagnosis of retinoblastoma was made. Associated nonocular conditions in these cases were not mentioned or are not pertinent to this discussion.

Of the group, all but 3 eyes were removed. Microphthalmos was evident in 12 eyes. Retrolental fibrous tissue and the hyaloid artery were shown in histologic sections in 23 eyes. In only 4 eyes was retinal detachment observed. Of these, the retina was detached nasally in 1 eye, in another it was detached eight years after the first ophthalmic examination, and in the other 2 eyes the retinas are described simply as detached by "albuminous material."

Thus it may be seen clinically that the disease called retrolental fibroplasia by Terry and the disease designated in the literature as connective tissue hyperplasia associated with a persistent hyaloid artery are apparently different conditions. They have the following signs in common: gray pupillary reflex, shallow anterior chamber, posterior synechias and microphthalmos in the newborn. Retrolental fibroplasia is bilateral and usually appears in premature infants. In the second disease, on the contrary, the hyperplastic mass associated with the persistent hyaloid artery is unilateral and is not related to prematurity. Vision in the other eye is generally good. The 18 cases from the Uni-

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zwei Brudern und Amotio retinae acq. bei Vater und Sohn und uber Pseudogliom mit Nekrose der Uvea und Retina beim Sohn eines Vaters mit Iritis, *Ztschr. f. Augenh.* **56** 155, 1925 (d') Lachman, G. L. Bilateral Hemorrhagic Detachment of Retina in New Born Simulating Glioma, *Am. J. Ophth.* **10** 164, 1927 (e') Wetzell, J. O. Pseudoglioma of the Retina, *ibid.* **24** 164, 1941

versity of Chicago Clinics presented in this paper are similar clinically to the cases reported by Terry, but they cannot be regarded as instances of retrolental fibroplasia associated with a persistent hyaloid artery

*Encephalic Dysplasia*—As far as I am able to determine, there are few cases of encephalic dysplasia reported in the literature which may be considered as coming under the classification of congenital encephalo-ophthalmic dysplasia. In a recent clinical case of retinal folds<sup>3</sup> the lesion was reported to be associated with microcephaly and mental retardation, and in another clinical case<sup>4</sup> a retinal fold occurred in one eye and a retinal detachment in the other. In at least 2 of the 5 cases<sup>5</sup> with lissencephaly there was no pupillary reaction to light. In the 1 case in which ophthalmoscopic examination was made no abnormality was visible.

A complete description of a patient having cerebral and retinal dysplasia was given by Wehrli.<sup>6</sup> The infant was delivered fourteen days prematurely with instruments because the membranes were ruptured. The other twin survived and remained healthy. The patient died at the age of 16 months of gastroenteritis. At autopsy the eyes were observed to be normal in size. The left eye was removed because ophthalmoscopic examination showed a small nodule in the retina near the disk. The fundus of the other eye appeared normal. Pathologic examination of the left eye revealed pronounced hypoplasia of the retina. The stratified layers were thin, and the cells were few and small. The hypoplasia affected mainly the outer neurons. The small tumor was composed of a double inner nuclear layer and many incompletely differentiated retinal cells, superimposed on an abnormally thin retina peripherally. Beneath the tumor the retina was irregular and distorted. The rest of the eye was normal. The child was hydrocephalic. The brain showed microgyria, macrogyria, heterotopias and small embryonal tumors of the ependyma. The spinal cord was normal. The disease in this case was like that in cases 9 and 10 of the present series.

#### REPORT OF CASES

Over sixty physicians have aided in the study of these cases. Without the assistance of Dr Douglas N. Buchanan, of the department of pediatrics, and Miss Miriam Norris, in the social service department of the University of Chicago, this study could not have been completed.

3 Gartner, S. Congenital Retinal Folds and Microcephaly, Arch Ophth 25 93 (Jan) 1941

4 Guerry, D. Congenital Retinal Folds, Am J Ophth 27 1132, 1944

5 Walker, A. E. Lissencephaly, Arch Neurol & Psychiat 48-13 (July) 1942

6 Wehrli, E. Ueber der Mikro- und Makrogyrie des Gehirns analoge Entwicklungsstörungen der Retina mit Besprechung der Epithelrosetten und der Pathogenese des Glioma, Arch f Ophth 60 302, 1905

All patients were repeatedly seen by me except for the eighth, who died twenty-four hours after birth. The eyes were usually examined while the child was under general anesthesia. In many cases the biomicroscope was employed.

CASE 1—M L, a white girl, was delivered by cesarean operation in the University of Chicago Clinics on Oct 29, 1937, after six and one-half months' gestation because the mother had toxemia of pregnancy. The placenta and uterus of the mother were normal microscopically. The weight of the child was 900 Gm, and the length was 37 cm. The circumference of the head was 35.6 cm. No physical abnormalities were found on examination. The child was kept in an incubator for three weeks and was treated for weakness and anemia in the hospital until Jan 6, 1938. On discharge she was in good health and weighed 2,495 Gm.

The father and mother were born in the Netherlands. The father, aged 41, had hypertensive heart disease. The mother, aged 44, had essential hypertension and belonged to a family with a tendency toward essential hypertension. Her fundi were normal in appearance after delivery. The patient was the result of a second pregnancy, the first child, a girl, was 18 years of age and healthy. No evidence of ancestral nervous or ocular disease was obtainable.

On April 27, 1938 the mother returned with the child to the University Clinics. When she had arrived home, she had incidentally noticed that the child, at the age of 9 weeks, was unable to see objects, but squinted, in bright sunlight. Examination by the pediatrician showed that the child, a small, premature infant, was normal except for the eyes. The blood count and urine were normal. The Wassermann reaction of the blood was negative. The child was referred to the eye clinic.

The eyes gave no reaction to light. Searching nystagmoid movements were observed. The external ocular movements were unrestricted. The lacrimal apparatus, lids and conjunctiva were normal. The right cornea was 9 mm, and the left 9 mm, in diameter. The anterior chambers were shallow. The pupils were dilated and fixed. A greenish mass, which was derived from the retina, was seen back of each pupil. The tactile tension of the right eye was moderately higher than normal, and that of the left eye was normal. A diagnosis of bilateral retinoblastoma was made. On May 3, 1938 the right eye was removed.

On May 19 examination of the left eye showed a collapsed anterior chamber, new vessels on the anterior surface of the iris, posterior synechias, a vascularized mass in contact with the posterior surface of the lens and a high tactile intra-ocular tension. On May 21 the left eye was removed.

On Oct 22, 1940 mental retardation was noticed. The Kuhlmann psychometric test gave an intelligence quotient of 41. Vocabulary and memory were poorly developed.

In December 1940, according to the report of another institution, two psychologists and a psychiatrist found the child well and not physically handicapped or mentally retarded except for what could be ascribed to the loss of sight, as determined by informal examinations. The weight was 10.9 Kg, and the circumference of the head was 47.5 cm.

According to the statement from the county coroner's physician, the child died on Feb 27, 1941, of a mass in the brain. The diagnosis was not specific but was indicative of cerebral disease or hydrocephalus.

*Pathologic Examination*—Right Eye (fig 1A). The ocular bulb displaced 2.25 cc of 4 per cent alcohol. The diameter of the bulb was 15.5 mm antero-

posteriorly and 15.5 mm transversely. The diameter of the cornea was 9 mm. The depth of the anterior chamber was 0.4 mm. The filtration angle was partly open. The canal of Schlemm was small and multiple channelled. The choroid and the sclera were normal. About one third of the posterior pigment layer of the iris around the pupil was adherent to the anterior capsule of the lens. The lens was normal. Remains of an embryonic vascular system around the lens were not present. Just behind the lens a few amorphous strands of vitreous were seen to fray out laterally and to extend as fibrils to the ciliary body and processes. The space posterior to this was quite empty, and only one or two capillaries were present in the central serial sections.

On the inner surface of the pigment epithelium of the retina occasional small clumps of proliferating pigment cells and many ghost cells were seen. In the macular region the ghost cells were fifteen cells deep in one small area. The retina was detached in an area extending from the disk to the ciliary body.

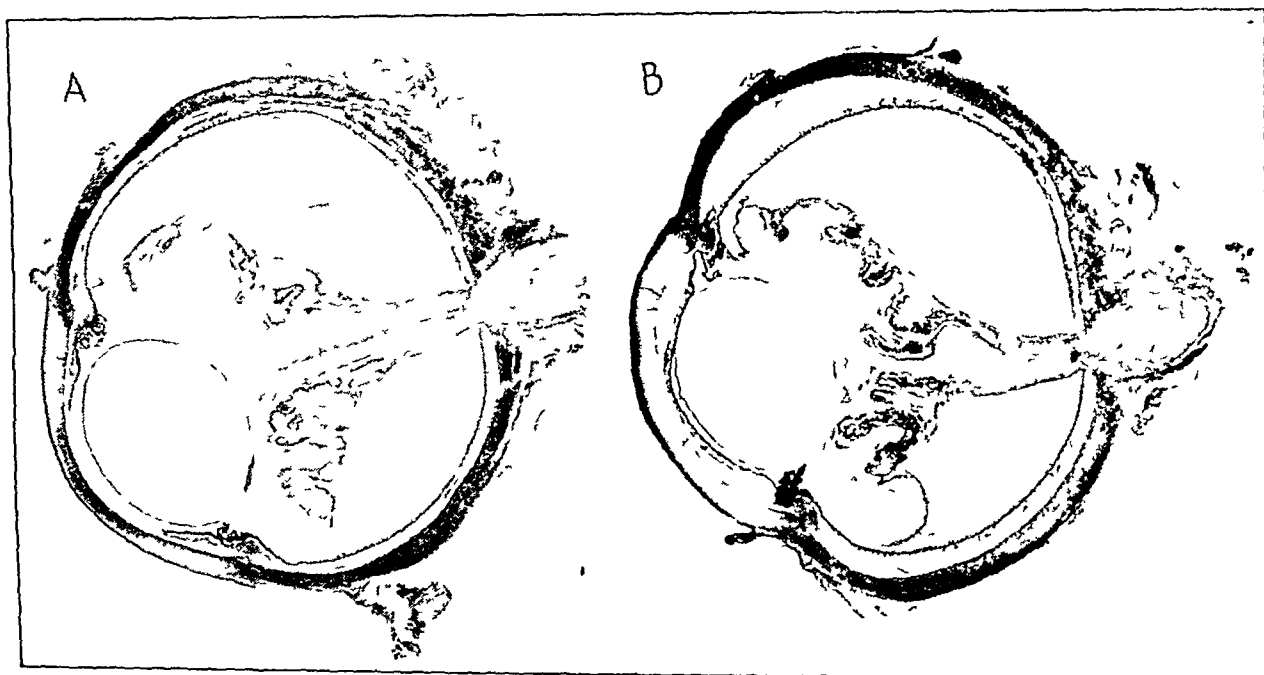


Fig 1 (case 1) —Cross sections of (A) the right eye and (B) the left eye. The lower part of B is the nasal side.  $\times 4$

The retinal mass had the shape of a blunt funnel. The stem leading from the optic nerve was not completely closed and was walled with the nerve fibers. The retinal vessels were in the middle of the stem. The peripheral tissue of the anterior part of the detached, atrophic, lobulated retina consisted of a layer of irregular neuroepithelium. In the lobules of the retina were many large, empty cystic spaces, the largest of which was about 2 mm in diameter. Scanty stratification of a few layers was noticeable in the disorganized, distorted retinal tissues. Several nests of pigment epithelial cells were noted externally on the posterior surface of the retina. The space between the pigment epithelium and the detached retina was filled with a serous exudate. A few lymphocytes were scattered throughout the retinal mass.

The optic nerve fibers were myelinated.

Left Eye (fig 1 B). The bulb displaced 25 cc of 8 per cent alcohol. It measured 15 mm anteroposteriorly and 15.5 mm transversely. The diameter of

the cornea was 9.5 mm. The filtration angle was partly open. The canal of Schlemm was patent. The anterior chamber was absent centrally and was 0.4 mm deep peripherally. The sclera was normal. About one half of the pigment epithelium of the pupillary part of the iris was adherent to the anterior surface of the lens. The central part of the pupillary space was filled with proliferating pigmented and unpigmented epithelial cells, corneal endothelial cells and connective tissue cells, which were adherent to the lens and to Descemet's membrane. The lens was normal. No vessels were seen on or around the lens. A serous exudate infiltrated the outer layers of the anterior half of the choroid. The retinal pigment epithelium was slightly irregular. A layer of ghost cells 20 to 200 microns thick and occasional small, proliferating nodules of pigment epithelial cells, sometimes surrounding a hyaline center, were lying on the inner surface.

The retina was detached from the disk to the first ciliary process. It was shaped like a short funnel. The central stalk was walled with partly organized retina, which surrounded the retinal vessels. No hyaloid artery was evident. The main mass of retina was lobulated by fusion. The lobule nasally possessed a thin glial wall, which was several cells thick. A few large cystic spaces, filled with areolar connective tissue, were present. On the temporal side the retina was fused to the first posterior ciliary processes. The atrophic retina showed irregular stratification, microcysts, pseudorosettes and tubes of cells. Just behind the posterior pole of the lens was an exceedingly thin, transverse, stratified connective tissue membrane, which frilled out laterally to join the retina, the ciliary body and the ciliary processes. Several very small vessels and capillaries were seen in the areolar tissue behind the membrane. An occasional lymphocyte and round cell were present in the retina.

The optic nerve was medullated.

CASE 2—D. S., a white boy, was born at the end of twenty-eight weeks' gestation, after a premature rupture of membranes, on July 10, 1939 in the University of Chicago Clinics. The mother, aged 31, was a primipara. No instruments were used in the delivery. The placenta was normal. The infant was in good condition. No signs of trauma, hemorrhage or other abnormalities were present. The child was placed in an incubator. On the eleventh day of life his weight was 955 Gm. He had no cyanosis, jaundice or convulsions. On discharge from the hospital, on September 19, the child weighed 2,535 Gm and was healthy.

The father was well, but his age was not obtained. The relatives and ancestors were free of ocular and nervous diseases.

On October 24 the child was examined in the pediatric clinic and was found to be normal for a premature infant.

On December 7 a gray mass was visible through the pupil of each eye. Physical examination showed no abnormalities except for the eyes. The blood count and the urine were normal. The Wassermann reaction of the blood was negative. The patient was referred to the eye clinic.

On December 13 an ophthalmic examination was made. No measurement of vision was obtainable. Bright light produced no blinking or movement of the eyes. Externally the eyes were normal. No restriction of action of the external ocular muscles was evident. The corneas were 9.5 mm in diameter.

The right cornea showed discrete, gray, deep opacities, 1 to 2 mm in diameter, distributed in seven loci equidistant from each other at the periphery and in a circle 2.5 mm from the limbus. The superficial reflex was brilliant. The rest of the cornea was clear. No corneal blood vessels or keratic precipitates were

seen The anterior chamber was almost obliterated by the blue, thin iris lying against the cornea The pupillary margin of the iris was ragged and was adherent to the posterior surface of the cornea No keratitic precipitates or iridic vessels were seen The pupil was 3 mm in diameter and was fixed The lens and the lateral anterior portion of the vitreous were clear The fundal reflex was gray An irregular, gray, granular mass, best seen with a +18 D lens, filled the posterior part of the vitreous cavity Two lateral vessels crossed in the mass radially No details of the mass were observed

The left cornea, 9.5 mm in diameter, was clear The anterior chamber was collapsed The blue, thin iris was flush against the posterior surface of the cornea The pupil was 5 mm in diameter and was fixed to light No posterior synechias were seen The lens was clear A red reflex was obtained nasally at the extreme periphery at 10 30 o'clock The rest of the fundus was obscured by a yellowish gray mass, which filled the cavity Several radial vessels in depressions passed to the center of the floating mass At the periphery of the mass, at 4 30 o'clock, was a small red blood clot, and at 11 o'clock, a group of fine vessels Only the anterior half of the bulb could be transilluminated The tension (Souter) was less than 10 mm in each eye

A tentative diagnosis of bilateral retinoblastoma was made

On December 18 the eyes were removed A course of twenty-four roentgen treatments was given to the orbits for possible extension of growth of the retinoblastomas

On May 31, 1940 the mother, after twenty-three weeks' gestation, had another premature infant, which was stillborn after premature rupture of the membranes Histopathologic examination revealed that the infant was a normal, previable fetus with normal eyes

On May 3, 1943 the psychologists and psychiatrists again examined the patient No physical or mental abnormalities except those referable to the eyes were evident The child was healthy and was becoming well adjusted to other children and to the home On July 9, 1945 his condition was unchanged

*Pathologic Examination—Right Eye* The anteroposterior diameter of the bulb was 17 mm and the transverse diameter 17 mm The bulb displaced 4 cc of 1 per cent alcohol The diameter of the cornea was 9.5 mm The filtration angle was partly open The canal of Schlemm was patent The anterior chamber was 0.5 mm deep The sclera was normal The pigment layer of the iris at the pupillary margin was adherent to the lens capsule The stromal layer gave off projections one to three cells thick, which passed over the pupil onto the lens The lens was normal No vestigial embryonic vessels around the lens were seen The choroid was engorged Anteriorly, near the ciliary body, the external lamellas were separated by a serofibrous exudate The pigment epithelium showed a few minute clusters of proliferating cells on the inner surface At the equator a patch of ghost cells, 3 mm in width, was seen on the pigment epithelium

The retina was detached from the disk to the ciliary body The stalklike central structure was constricted in the middle The chief mass of retina was behind the lens and was fused to the posterior ciliary processes The anterior surface of the mass was 11 mm in diameter The branches of the central retinal vessels were enclosed in the stalk A small part of the atrophic retina was incompletely stratified A few large and many small tubular pseudorosettes were seen in the posterior half of the retina A few scattered small masses of red blood cells were present in the retinal strata of one lobule and in a few tubular



pseudorosettes. A few leukocytes, plasma cells and phagocytes were disseminated throughout the atrophic retina. The space between the retina and the pigment epithelium was filled with a serous exudate.

Only a few, fine capillaries were seen in the dense transverse vitreous membranes adherent to the middle of the posterior surface of the lens capsule. Lateral to the band of membranes was an areolar vitreous structure.

The optic nerve was apparently normal.

**Left Eye (fig 2A)** The diameter of the bulb was 17.25 mm anteroposteriorly and 16.5 mm transversely. The bulb displaced 4 cc of 1 per cent alcohol. The diameter of the cornea was 9.5 mm. The canal of Schlemm was small and was covered partly by the trabeculae in the incomplete opening of the filtration angle. The anterior chamber was 1 mm deep. It

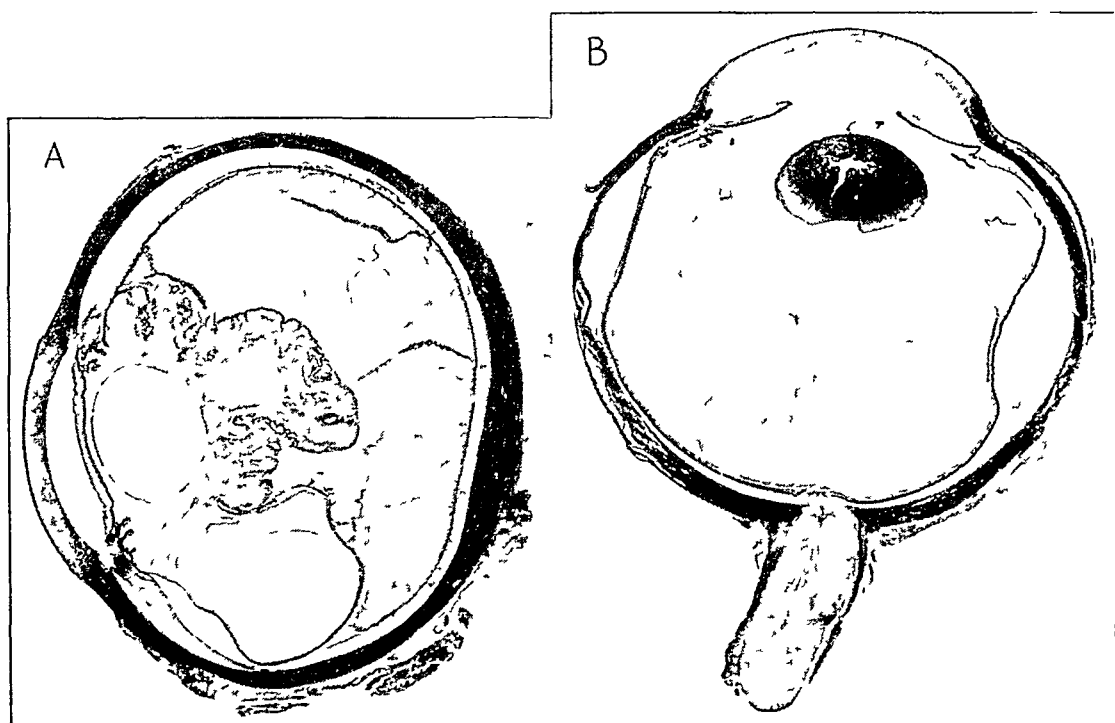


Fig 2—*A* (case 2), cross section of the left eye, showing detached retina and large nasal retinal cyst, *B* (case 3), cross section of the right eye.  $\times 4$

contained a small quantity of serous exudate. The sclera was normal. The pupillary pigmented border of the iris was adherent to the anterior capsule. No capillaries and cellular veils were seen on the lens. The lens was normal. The muscle fibers of the ciliary body were not quite completely developed in numbers and in position. The external lamellae of the choroid adjacent to the pars plana contained a serofibrinous exudate. The retinal pigment epithelium showed a few small nodules of proliferating pigment cells. An occasional ghost cell was close to the pigment epithelium. The space between the retina and the pigment epithelium was filled with a serous exudate.

The flower-shaped mass of retina was detached from the disk to the first ciliary process. The main mass of the retina was behind the iris and the lens and was focused laterally to the pars plana. The posterior part of the central

stalk contained the retinal vessels, optic nerve and glial fibers. The anterior mass of retina was lobulated by fusion. Several large lobules were stratified, but the others were irregular masses of retinal cells and glial tissue. A few pseudorosettes and tubules of stratified retinal cells were seen. Microcysts in the masses of cells were present. A dense and layered amorphous membrane covered the posterior central third of the lens capsule. Laterally the membrane fused with areolar tissue and posteriorly with glial tissue. Only a few capillaries were evident in the tissue next to the lens. The retinal mass possessed no large vessels. A part of the retina, forming a sac 6 mm in diameter, projected nasally and posteriorly from the central postlental retinal mass. The unorganized, atrophic retina and glial tissue formed the thin wall of a cyst, containing a serous fluid. The outer part was fused to the choroid for 4 to 6 mm.

The optic nerve was apparently normal.

CASE 3—R. R., a white boy, was born in the University of Chicago Clinics on Feb. 23, 1943, after thirty-one weeks' gestation, of a first pregnancy. The placenta was normal. The cause of prematurity was unknown. The other infant of the twin birth died forty-eight hours after delivery.

The child was in good condition and showed no evidence of traumatic injury. He required no artificial revival. The eyes appeared to be normal. The child was placed in a Hess bed with a constant supply of oxygen. At the age of 13 days he weighed 1,100 Gm. During the first three months of life he barely survived infections of the skin, bilateral otitis media and repeated attacks of cyanosis. The infections were treated with sulfathiazole and sulfadiazine. He was discharged from the hospital on May 4, 1943, with a weight of 3,000 Gm and with a diagnosis of hemangioma of the occiput, systolic cardiac murmur and congenital umbilical hernia.

The father, aged 21, and the mother, aged 20, had always been healthy. Both parents were born in Chicago. Their families had no hereditary ocular or nervous diseases. The Wassermann reaction of the mother was negative.

On May 27 the child was returned to the pediatric clinic, where the pediatrician made a diagnosis of anemia, incipient vitamins C and D deficiency and a mass in the left ocular fundus.

*Ophthalmic Examination*—On May 28 an ophthalmic examination was made, although the mother noticed nothing unusual about the child's eyes. Externally the eyes were normal. The corneas were clear.

*Right Eye* The anterior chamber was of normal depth. The pupil was round, regular and reactive to light. The lens was clear. The fundus showed a pronounced anomalous distribution of the retinal blood vessels. The vessels seemed to be almost entirely on the temporal side of the disk. The retina had the abnormal color of pink porcelain. The macular reflex was absent.

*Left Eye* The anterior chamber was shallow. The pupil was fixed by irregular posterior synechias. Homatropine dilated the pupil irregularly. The lens was clear. The retina was detached and floated as a billowy, vascular gray cloud just behind the lens. A tentative diagnosis of retrolental fibroplasia of the left eye was made.

On June 4, 1943 the child died, while he was on the way to the hospital. He weighed 2,930 Gm.

The pathologic diagnosis was acute enteritis, emaciation, umbilical hernia and small hemangioma of the scalp. The brain weighed 433 Gm and was normal histologically. The eyes were studied separately.

*Histologic Examination*—Right Eye (fig 2*B*) The anteroposterior diameter of the eye was 16 mm. The cornea was 8.5 mm in diameter and was normal. The sclera appeared normal. The anterior chamber was 2 mm deep. The trabeculae partly filled the filtration angle. The pupil was 3 mm wide. A few cells of the pigmentary border of the pupil were adherent to the anterior surface of the capsule. The lens was normal. No evidence of embryonic vascular structure was seen in the iris or the lens. The ciliary body was normal.

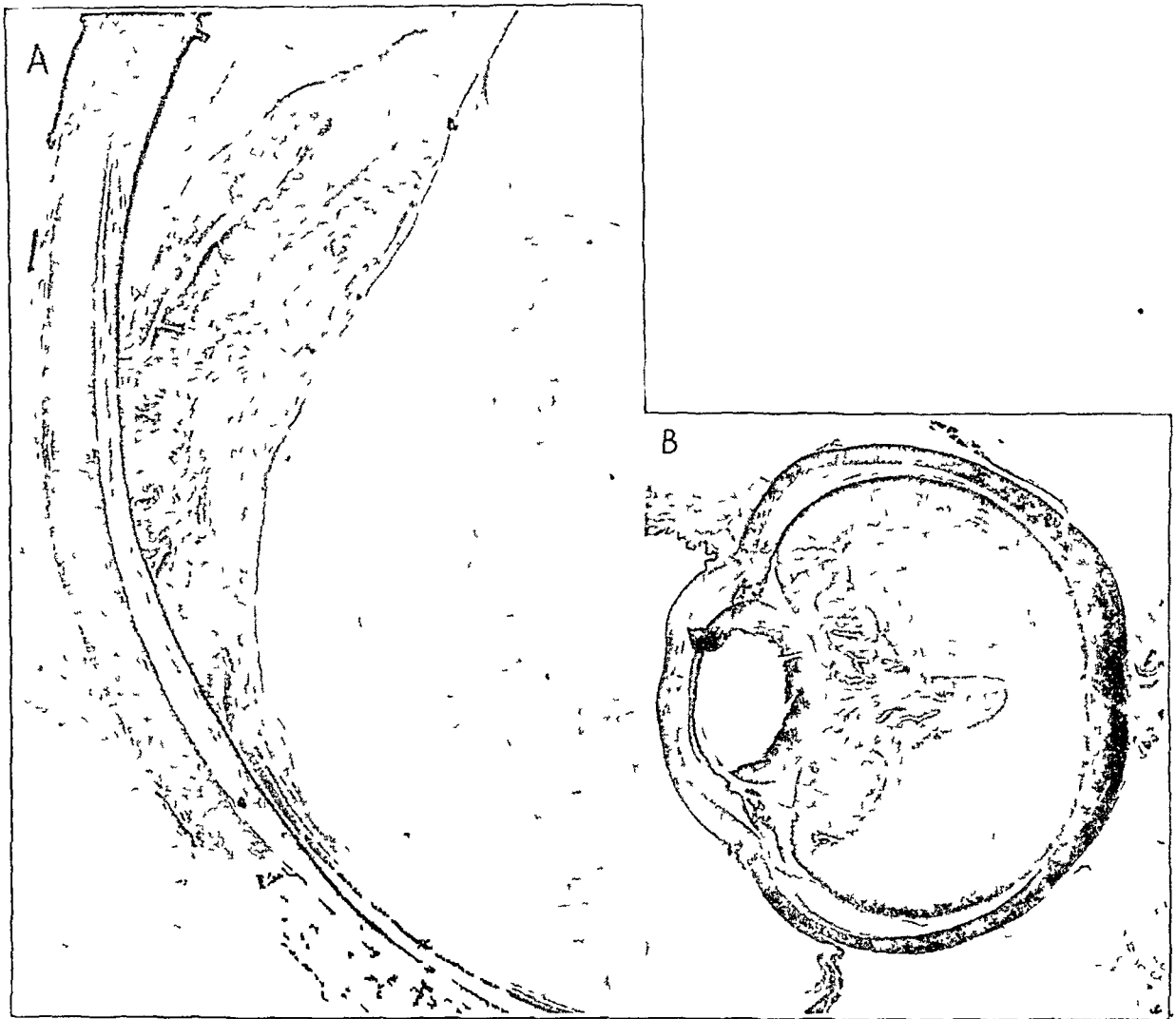


Fig 3 (case 3)—*A*, cross section of the retina near the ora serrata, showing hyperplasia on the nasal side of the right eye, *B*, cross section of the left eye ( $\times 4$ )

In one segment nasally, beginning 3 to 4 mm from the ora serrata, the retina projected as a plicated, unorganized growth, extending from the ora serrata toward the lens in the shape of a half-moon, with the convexity outward (fig 3*A*). The mass was 8 mm wide and 2 mm thick. The double internal limiting membrane of the retina joined the zonular ligaments. The central parts of the folds, where

the retina was detached, were filled with an albuminous fluid. The retina was arranged in stratified and unstratified nodules, tubes and rosettes of cells of the neuroepithelium. Large areas of proliferating neuroglia were seen.

The retina adjacent to the overgrown portion of the retina for about 6 mm showed multiple, irregular-sized spaces between the cells of the inner and the outer nuclear layer. Below the middle of this area of the retina, the choroid showed conspicuous round cell infiltration. In the center, 2 mm of the retina was detached and elevated as a mound, over an albuminous fluid. Many scattered red blood cells and a few lymphocytes and macrophages were seen above the pigment epithelium.

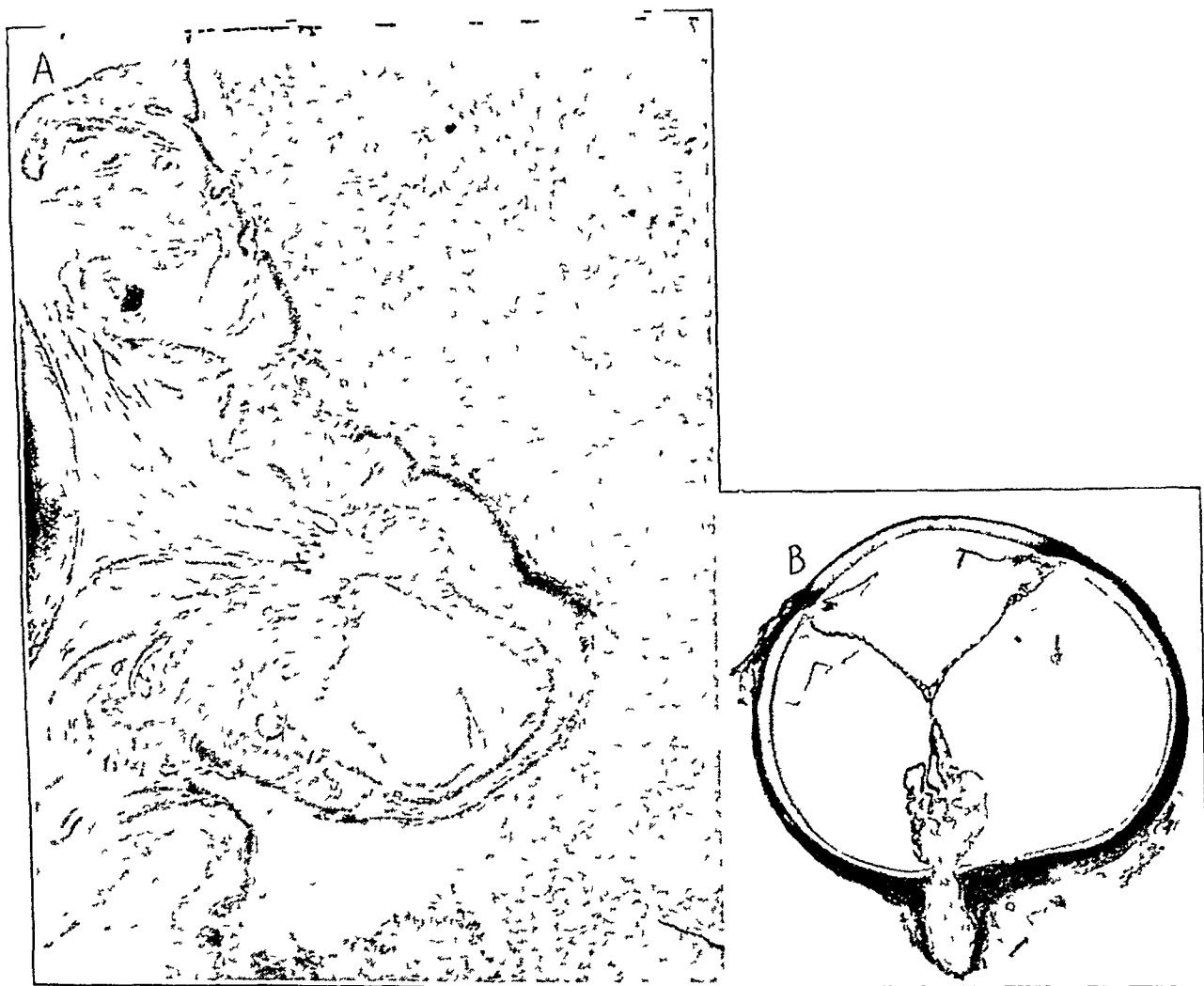


Fig 4—*A* (case 3), cross section of the left eye behind the lens, showing absence of hyaloid system and of the postlental mesodermal fibrosis, *B* (case 6), cross section of the left eye ( $\times 3\frac{1}{2}$ )

in the fluid. The retina above was thickened chiefly by the large amount of glial cells and fibers. The inner and outer layers of nuclei were irregularly arranged. The nuclei were filled with fine granules. The nuclei were fewer and were spaced so as to show many varied, noncystic gaps. The nerve fiber layer of most of the retina appeared to be thicker and to show more neuroglial nuclei and less ganglionic nuclei than normal. In short, the retina was hypoplastic and hyperplastic. The disk was free from vestigial remains of the hyaloid vascular system. The optic nerve was apparently normal.

Left Eye (fig 3B) The volume of the bulb was 35 cc The diameter was 15 mm anteroposteriorly and 15 mm transversely The cornea measured 9 mm vertically and 10 mm horizontally The epithelium was thinner in the middle of the cornea The filtration angle was partly open The canal of Schlemm was patent The anterior chamber was 0.5 mm deep in the center The sclera was normal The pigment epithelium of the pupillary border of the iris was adherent to the anterior capsule A few layers of cells from the stroma of the iris passed onto or over the anterior surface of the lens in the pupillary space No vessels appeared on the anterior capsule The choroid was normal The cells of the pigment epithelium of the retina were slightly pigmented and irregular in size Many ghost cells were present on the surface of the epithelium

The retina was detached from the disk to the first ciliary process It was shaped like a mushroom, with a stalk attached to the optic nerve and with an inverted head lying in contact with the lens, across the anterior portion of the vitreous cavity The stalk was formed by glia, nerve fibers and a few large vessels The lobulated retinal mass was formed by fusion of folds of the detached retina The borders of the lobes were composed of fairly well stratified layers of cells In one segment of the distorted retina many minute, old hemorrhages and several the size of a pinhead were seen

Behind the lens was a small, flat mass of vitreous fibrils confluent with glial tissue of the retina Only a few capillaries were present in the glial or the connective tissue No embryonic vascular tree or hyaloid artery was seen behind the lens (fig 4A)

The optic nerve was apparently normal

CASE 4—M S, a white girl, was born Dec 22, 1937, after a gestation of twenty-eight weeks The cause of the prematurity was unknown A midwife aided in the delivery The placenta was not examined The weight on the sixth day was 1,065 Gm On the day of birth the infant was admitted to the University of Chicago Clinics with intermittent cyanosis and was placed in an incubator On Feb 25, 1938 the infant, healthy and weighing 2,790 Gm, was discharged from the hospital

The father was 27 and the mother 21 A brother, aged 3 years, and a sister, aged 1 year, were well On March 26, 1938 the mother brought the child to the University of Chicago Clinics for treatment of a "bulging" left eye, which she had noticed three days before Physical examination revealed a normal premature child The circumference of the head was 34 cm The blood count and the urine were normal

The conjugate movements of the eyes were normal The right eye was slightly enlarged The cornea was clear The anterior chamber was shallow, particularly on the temporal side The pupil was oval and irregular A greenish gray mass with blood vessels on its anterior surface, was just behind the lens

The left eye was more prominent and larger than the right eye The cornea was enlarged and slightly cloudy The epithelial reflex was dull The anterior chamber was shallow The pattern of the iris was blurred The radial vessels on the iris were engorged The pupil was irregular and was 5 mm in diameter Just behind the lens an irregular, greenish gray mass was seen The tactile tension was above normal

A diagnosis of bilateral retinoblastoma was made

On April 5, 1938 a bilateral enucleation was done Roentgenologic treatment of the orbits was given

On Nov 10, 1942 examination showed definite mental retardation which was not related to loss of vision The child was well developed but undernourished She

was unable to use words or to walk unassisted. She was kept under observation until March 13, 1943. On Aug. 15, 1944 she was admitted to an institution for the feeble-minded.

*Pathologic Examination—Right Eye* The bulb was 17.5 mm in diameter anteroposteriorly and 16.5 mm transversely. The cornea was 10 mm in diameter. The cornea was thinner than normal. The filtration angle was partly closed as a result of anterior displacement of the peripheral part of the iris. The canal of Schlemm was collapsed. The anterior chamber was shallow. The pupillary part of the iris was adherent to the anterior surface of the capsule. The sclera was thin. The lens was normal. The vessels of the ciliary body, iris and choroid were engorged. Anterior to the equator the choroid was distended by a hemorrhage. On the surface of the retinal pigment epithelium were proliferating pigment cells and ghost cells. The proliferation of neuroepithelial cells tended to fuse the processes together. Anteriorly, double layers of pigment epithelial cells formed large hemorrhagic cysts.

The atrophic retina was detached from the disk to the first posterior ciliary process. The main mass of the retina was shaped like a flower, with a central stalk joining the optic nerve. Small tubes, spheres and layers of stratified retinal cells were present at the periphery of the anterior portion of the retinal mass. Centrally, glial and connective tissue was evident. Posteriorly, the retina was covered with a layer of epithelial and connective tissue cells. Large hemorrhagic cysts were occasionally enclosed. A few leukocytes, plasma cells and phagocytes were scattered throughout the retina. The space between the retina and the epithelial layer was filled with exudate. Posteriorly, the lens capsule was adherent to a thin, transverse, laminated hyaline membrane, the lateral fibrils of which were attached to the ciliary processes and the ciliary body. Posterior to the membrane a small pyramidal space was filled with areolar tissue, which possessed a few capillaries. The stalk consisted of glial and connective tissue, nerve fibers and several large blood vessels. An irregular layer of hyalinized red cells was present beneath the outer wall of the stalk. The interretinal and intraretinal spaces and the anterior and posterior chambers were filled with a hemorrhagic exudate.

The optic nerve was partly atrophied.

*Left Eye* The diameter of the bulb measured 19 mm anteroposteriorly and 16.5 mm transversely. The diameter of the cornea was 10 mm. The corneal endothelium was flattened. The anterior chamber was 1.8 mm deep and contained exudate. The sclera was thin. Peripherally, most of the iris touched or adhered to the cornea. The pupillary part of the iris was adherent to the anterior surface of the lens. A serofibrinous exudate, containing erythrocytes, filled the space behind the iris. The lens was normal. The vessels of the choroid and iris were engorged. A large hemorrhage distended the choroid in the region of the ora serrata, where it broke through into the space behind the retina. A few lymphocytes and plasma cells were present in the choroid near the ciliary processes and the pars plana. The pigment epithelium was thickened, multiple layered and distorted over the ora serrata and near the equator. Near the ciliary body it formed strands, islands and cysts in the adjacent retina.

The retina was detached from the disk to the ciliary body. The long, narrow stalk, leading from the anterior mass of retina to the optic nerve, was about 1 mm in diameter. It consisted of glial and connective tissue, with a few nerve fibers and small vessels. In its center was a large hemorrhagic cyst. The pyramidal mass of the retina lying behind the lens was fused laterally to the ciliary processes by areolar connective tissue and by masses of proliferating neuroepithelial cells. The middle of the posterior surface of the lens was adherent to a very thin layer of

hyaline tissue. No vascularization of this layer was seen. The main mass of retina showed empty and hemorrhagic cysts, hyalinized erythrocytes and occasional stratified layers of retinal cells. No folding or lobulation was evident. The vessels were small and few. A hemorrhage was spread over the posterior surface of the retina. The space between the pigment epithelium and the detached retina was filled with a hemorrhagic exudate. It contained fibrin and small masses of hyalinized red cells and clusters of epithelial cells.

The optic nerve was partly atrophic.

CASE 5—A S., a white girl, was born in an outside hospital July 14, 1939, after seven months' gestation, with a weight of 1,550 Gm. No instruments were used in the delivery. No trauma occurred. The cause of the premature birth was placenta previa. The infant was jaundiced, but not cyanotic, for a short time after birth. She was kept in an incubator in the hospital for two months after delivery. At the end of six months she weighed 6,250 Gm.

The mother was 26 and the father 30. The only previous pregnancy terminated in the delivery of a 6.5 month, premature infant, who died in two hours. The cause was placenta previa. The family history suggested no ocular or nervous diseases except for spinal bifida in a third cousin.

Immediately after the child was brought home from the hospital the mother noticed the white pupil in each eye. An ophthalmologist and the family physician, on examination of the eyes, suspected glomas.

On Dec. 6, 1939 the child was given a medical, neurologic and ocular examination in the University Clinics. The condition was normal except for the eyes. The blood count and the urine were normal. Roentgenographic examination showed that the skull, chest and optic foramina were normal. The right eye showed a clear cornea. The left cornea gave a dull epithelial reflex. The anterior chambers were shallow. The irises were thin and slightly atrophic. The pupils were 3 mm in diameter. With instillation of atropine, the pupils dilated irregularly, the right dilating horizontally to 5 mm and the left to 5.5 mm. Just behind the lens in each eye a greenish white, homogeneous mass was seen. In the left eye a reddish brown area, noted later to be a hemorrhage, was seen off center temporally on the mass behind the lens. A diagnosis of bilateral retinoblastoma was made.

On December 8, before the operation, tension (Souter) was 12 mm in the right eye and 36 mm in the left eye. The left eye was enucleated. The right eye later showed intermittent glaucoma. Because of the pain, the right eye was enucleated on Jan. 30, 1940. At this time the circumference of the head was 42 cm. When the child was examined, on Aug. 3, 1943, she was healthy and active. There were no signs of mental retardation. On May 25, 1944 the artificial eyes were refitted. On Oct. 20, 1945 the condition of the child was unchanged, but she was erratic in her behavior.

*Pathologic Examination*—Right Eye. The diameter of the bulb was 18.5 mm anteroposteriorly and 19 mm transversely. The bulb displaced 3.75 cc of 4 per cent alcohol. The diameter of the cornea was 12 mm. The volume of the anterior chamber was decreased by the peripheral anterior synechias and by the adhesions of the pupillary half of the iris to Descemet's membrane. The chamber was filled with a light exudate. In most sections the root of the iris covered the filtration angle. The canal of Schlemm was collapsed. The sclera was normal. The pupillary portion of the iris was adherent to Descemet's membrane. The pupillary space was filled with a membrane of thin connective tissue, arising from the iris. The pigment epithelium of the posterior part of the iris formed small and moderate-sized cysts. The periphery of the iris was thin and was generally fused to the cornea. The central third of the iris was adherent to the anterior capsule of the

lens The lens was normal The pigment epithelium of the retina showed many proliferating clusters and layers of pigment cells A heavy exudate filled the space between the pigment epithelium and the detached retina It contained a multitude of red cells in various stages of disintegration and many ghost cells, particularly near the pigment epithelium

The retina was detached from the disk to the ciliary body It formed a stalk which joined the optic nerve The main mass of the retina was consolidated into a flat pyramid, lying against the lens and the ciliary processes The ora serrata was covered with a disorganized layer of pigment epithelial cells and strands of retinal, glial and connective tissue The ciliary processes showed overgrowth of epithelial cells, frequently fused with connective and glial tissue The space between the ciliary processes and the displaced iris was filled with a serofibrinous exudate and new connective tissue fibrils A transverse sheet of amorphous, striated fibrous tissue was adherent to the posterior capsule of the lens Laterally it became fibrillar and joined the overgrown epithelium of the ciliary processes Posteriorly it was confluent with the retina The retina was grossly plicated, atrophic and gliosed A thin-walled intraretinal cyst, 1 mm in diameter, was seen centrally behind the lens Regular stratification was absent A few lymphocytes, plasma cells and phagocytes were seen in the retina and in the choroid

The optic nerve was slightly atrophic

Left Eye The diameter of the bulb was 20 mm anteroposteriorly and 19.5 mm transversely The bulb displaced 4 cc of water The cornea was 11.5 mm in diameter The anterior chamber was absent centrally and was about 1.5 mm deep laterally The filtration angle was closed by the peripheral anterior synechias The canal of Schlemm was collapsed The sclera was slightly thinner than normal The lens was normal One-half the pupillary portion of the iris was adherent to the lens At the pupillary border a few short filaments of connective tissue from the iris were adherent to the lens capsule The iris and lens were in contact with the middle third of the posterior surface of the cornea, where the iris was adherent to Descemet's membrane The choroidal, ciliary and iridic vessels were engorged The ciliary processes were thin and atrophic and were surrounded with newly formed fibrin The choroid and ciliary processes showed a few small areas of infiltration with lymphocytes, plasma cells, mononuclear cells and eosinophils The pigment epithelial cells were irregular in size and occasionally in clumps A few proliferating and disintegrating pigment epithelial cells were observed in portions of the retina, and many were noted in and around the region of the pars plana and the ciliary processes

The retina was detached from the disk to the ora serrata The main mass of the retina was behind the lens, where it lay against a thinly stratified, amorphous transverse membrane Laterally the membrane was joined to the ciliary processes by thin filaments The proliferating masses of glia and epithelial cells were fused to the ciliary processes and to the sides of the retina Posterior to the lens two intraretinal cysts filled with red blood cells were present in the retina A large cystic space, 12 mm wide and 4 mm deep, behind the main mass of the retina was filled with exudate Its wall was composed of a thin layer of gliosed, unorganized retina Its base was joined to the optic nerve by a stalk of gliosed nerve fibers The gliosed atrophic retina behind the lens showed slight evidence of stratification Only a few small circular nests of stratified cells around a cyst were seen The space around the stalk was filled with exudate, containing, anteriorly, disintegrating red blood cells and, posteriorly, a dense mass of whole red blood cells

The optic nerve contained more connective tissue than normal



CASE 6—J K, a white girl, was born in another hospital on March 4, 1938, three and one-half weeks prematurely, with a weight of 2,840 Gm. The cause of the premature delivery was unknown. The labor under ether anesthesia was not prolonged. No instruments were used. The child was in good condition and was without injury. Postnatal revival was unnecessary. There was no jaundice after the first day of life. For the next three weeks she was kept in an incubator under an oxygen tent for recurrent cyanosis. On her discharge, at 3 weeks of age, her weight was 2,650 Gm.

The father, aged 32, and the sister, aged 17 months, were healthy. The mother, aged 26, had diabetes, and her sister has tuberculosis. No history of nervous or ocular disease in the family was obtained.

On March 29 the infant was brought to the University of Chicago Clinics for an examination. She was undernourished and underdeveloped. Complete blood counts and the urine were normal. Roentgenologic examination of the skull and chest showed no abnormalities. A diagnosis of malnutrition and retinoblastoma of the left eye was made by pediatricians.

A more complete ocular examination was made on April 15. The mother had observed no abnormalities of the eyes or of vision. The left upper lid drooped slightly but moved normally. The eyes tended to converge. The right eye seemed to be the useful one. The left bulb was slightly smaller than the right. The conjunctivas and corneas were clear. The pupils dilated to 5.5 mm with atropine. In the right eye the anterior chamber was shallow. The iris was normal. The lens was clear. On the posterior surface of the lens a small remnant of the hyaloid artery was visible. The fundus was best seen with a -20 D lens. The appearance of the fundus suggested incomplete albinism. The retinal vessels were visible posteriorly over the yellow fundus. The choroidal vessels were prominent over the equatorial region. The disk was chalk white and flat.

The anterior chamber of the left eye was shallow. The iris showed a few dilated radial blood vessels. The lens was clear. A greenish gray mass without noticeable blood vessels was best seen just back of the lens with a +10 D lens. A diagnosis of retinoblastoma of the left eye was made.

On April 14 the child had overcome recurrent cyanosis and began to recover lost weight. The circumference of the head was 36 cm. On April 24 the sagittal sutures were found to be separated. Hydrocephalus was developing as the child became less dehydrated.

On May 3 the left eye was removed. Six weeks later, when the child was last seen by an ophthalmologist, pronounced hydrocephalus was present. The circumference of the head was 42.2 cm. The fundus of the right eye was best seen with a -20 D lens. The disk was white, and the fundus was albinotic from the lack of melanotic pigment. Nasally, the retina was grayish yellow as seen at the equator and greenish peripherally. No masses or plaques were seen. The child was discharged from the hospital on June 6.

On July 29 the child was having frequent recurrent attacks of choking and cyanosis. Her weight was 5,730 Gm.

The coroner's physician reported that on Aug. 21, 1938 the patient died, with extreme congenital hydrocephalus. No tumor was evident in the optic nerve or the cranium. The cerebral cortex was less than 1 cm thick. The ventricles were widely dilated. The aqueduct between the third and fourth ventricles was blocked by fibrous adhesions.

*Pathologic Examination*—Left Eye (fig. 4B). The bulb measured 16.5 mm anteroposteriorly and 17 mm transversely. It displaced 3 cc of 4 per cent alcohol. The cornea was 10 mm in the vertical diameter and 11.5 mm in the horizontal

diameter. Its appearance was normal. The canal of Schlemm was covered by the trabeculations of the slightly opened filtration angle and by the root of the iris. In many sections anterior displacement of the root of the iris and the ciliary body was seen. The anterior chamber was 1 mm deep and was filled with exudate. The sclera was normal. The pigment epithelium of the pupillary border of the iris was adherent to the lens capsule. Projections of the iris stroma extended a short distance into the pupillary space and also around the pupillary border to the anterior surface of the capsule behind the iris. Small vessels passed from the surface of the iris over the pupillary space and also onto the capsule back of the iris. The lens and choroid were normal.

The retina was detached from the disk to the ora serrata. The shape of the retinal mass was like that of a lobulated funnel, with its stem attached to the optic nerve. The conical part was tapered to form a 90 degree angle and was composed of a thickened, irregular layer of retina. The apex of the cone was attached by a thin, short stem to a large, round mass of folded retina, which was closely joined to the optic nerve. The retina behind the lens was adherent to one side of the posterior capsule for 1.5 mm and was also fused to a few ciliary processes on the same side. Some lobules of the retina were stratified. The bacillary layer formed tubular pseudorosettes. Large and small cystic spaces occurred in some lobules in all strata. The retinal cells of these layers were irregularly arranged and were frequently absent. A few large vessels were present in the stem of retina connecting the disk with the mass of retina.

The space between the retina and the lens contained a few fine fibrils of connective tissue and no blood vessels. Few or no remains of the vitreous were visible. The pigment epithelium was regular except for a few small masses of proliferating cells. The space between the detached retina and the pigment epithelium was filled with a pink-staining material, containing few red blood cells. Near the anterior retinal mass and the ciliary body the number of red blood cells was greatly increased.

The optic nerve was apparently normal. The lamina cribrosa was in place.

CASE 7—G. D., a white boy, was born Oct. 14, 1937, with a questionable gestational age of 6.5 months. The weight at birth was 1,835 Gm. The circumstances concerning delivery are unknown. On the day of birth the infant, who appeared normal and in fair condition, was brought to the hospital and placed in an incubator. On the second day oxygen was used to combat the cyanosis. On two occasions, for one day, the infant was moderately jaundiced. After fifty days the child was discharged from the hospital, with a weight of 2,625 Gm.

The mother was 22 and the father 30 years of age. The pregnancy was the first. The mother had a cough and had lost considerable weight. The child's great-grandfather and great-aunt had had tuberculosis. There was no history of nervous or ocular disease in the family.

On May 10, 1938 the child was admitted to the University of Chicago Clinics for an ophthalmic examination. Three months previously the mother had noticed that the right eye was larger than the left eye and that the head was rapidly enlarging. The circumference of the head was 42.5 cm. Except for the eyes, the child appeared to be normal. The blood and urine were normal. The Wassermann reaction of the blood was negative. Roentgenographic examination of the skull and optic foramina showed no abnormalities. No mental retardation was evident.

*Ophthalmic Examination* (May 13).—The child had a tendency to hold his fist over the right eye, which was more prominent than his left eye. The left eye turned in 25 degrees. Only the right eye followed light and gave a pupillary reaction to light.

**Right Eye** The fundus was best seen with a  $-20$  D lens after the pupil was dilated with atropine to 7 mm. The disk was pale. The central vessels were displaced temporally in an anomalous manner. The color of the fundus was that of a blond or partially albinotic person. No retinal mass was seen.

**Left Eye** The cornea and lens were clear and the anterior chamber was deep. A greenish gray mass, over which a few retinal vessels passed, was seen behind the lens on the nasal side. A diagnosis of retinoblastoma of the left eye was made.

On May 24 the left eye was again examined. The iris and lens were now displaced forward, and the anterior chamber was collapsed. The tactile tension was normal. The disk was best seen with a  $-20$  D lens, but the finer picture of the disk and fundus was blurred. The visible background was albinotic. A dense opacity in the vitreous extended forward from the disk. In the periphery, particularly nasally, a greenish white mass was noted. An enucleation of the left eye for probable glioma was done.

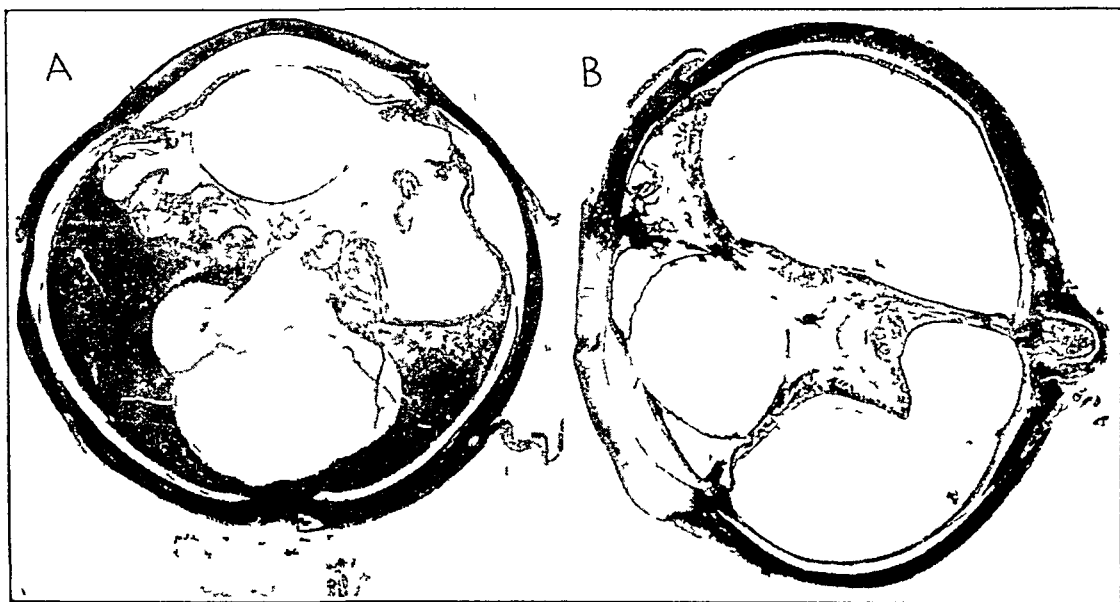


Fig 5—*A* (case 7), cross section of the left eye ( $\times 4$ ), *B* (case 8), cross section of the right eye ( $\times 5$ )

**Course**—On May 13, 1941 the right eye was reexamined. Vision was limited to large moving objects. A fine nystagmus was noticeable. The fungus was unchanged. The child was healthy and active mentally.

The child was still living in July 1944.

**Pathologic Examination of Left Eye** (fig 5*A*)—The bulb displaced 3 cc of 12 per cent alcohol. It measured 17.5 mm in the anteroposterior and 17.5 mm in the transverse diameter. The cornea was 9 mm in diameter. The anterior chamber was 1 mm deep. The filtration angle and the canal of Schlemm were open. The sclera was normal. One third of the pupillary portion of the pigment layer of the iris was adherent to the lens. The lens was normal. No capsulopupillary membranes or vessels were seen. The choroid was normal. The pigment epithelium of the retina was roughened. On the inner surface of the retina a few phagocytes, proliferating epithelial cells, clumps of pigment cells and ghost cells were

present. The space between the pigment epithelium and the retina was filled with exudate, containing scattered red blood cells.

The greatly atrophic retina was detached from the optic nerve to the base of the first large ciliary process. The main mass of the retina was in the anterior third of the vitreous chamber. The mass laterally consisted of a thin layer of unorganized retina, the anterior lateral ends of which extended toward the back of the lens. The stalk was short, about 5 mm long. On one side of the stalk, in the posterior third of the vitreous cavity, a cyst with a thin wall of retinal tissue, which was chiefly glial tissue, was fused to the posterior surface of the retina. It was filled with a noncellular exudate. The main retinal mass showed many large and a few small cysts filled with fibrin or fine connective tissue, a few tubular rosettes, slightly stratified retinal tissue and a few small blood vessels. Just behind the lens a thin layer of amorphous fibrous tissue lay transversely. The fine fibrils at the periphery of this layer extended to the posterior ciliary processes. The retina was fused posteriorly for about 2 mm to the middle of the layer. A large space with a few filaments of connective tissue was present on each side posterior to the area of fusion. Only a rare capillary was seen in this area.

The optic nerve was apparently normal.

CASE 8—B. K., a white infant, died twenty-four hours after delivery in another hospital. The mother, a 24 year old primipara, was unusually large at full term. Roentgenographic examination showed a large fetus with a large head. Cesarean section resulted in the birth of a hydrocephalic infant with bilateral talipes equinovarus. The suboccipitobregmatic measurement was 41 cm and the occipitofrontal 47 cm.

The eyes were examined eighteen hours post partum. The microphthalmos was bilateral. The eyes showed extreme convergence. The pupils were of medium size and inactive to light. Oblique illumination of the pupils gave yellow reflexes. Intraocular tumors were suspected.

Autopsy revealed a thin, friable dura. A large amount of clear fluid escaped, and the brain substance collapsed to a small, shapeless, structureless mass. The cerebrum and cerebellum were not distinguishable.

The microphthalmic right eye was removed for study. The bulb had a volume of 2 cc and measured 14 mm in the anteroposterior and vertical diameters and 15 mm in the horizontal diameter. No gross abnormalities were seen.

*Histologic Examination of Right Eye* (fig 5 B).—The eye was 13 mm in the anteroposterior and 15 mm in the horizontal diameter. The bulb displaced 2 cc of 1 per cent alcohol. The cornea was 7 mm in diameter. The epithelial layer was three to four cells thick. The sclera was normal. The anterior chamber was 1.5 mm deep and was filled with an amorphous exudate. The filtration angle was beginning to open. The canal of Schlemm was not seen in every section. The outer half of the temporal side of the iris was flush against, but not adherent to, the cornea. The pupillary pigment border of the iris was adherent to the lens capsule. A thin veil of iris stroma projected partly over the pupil. A few persistent capillaries from the iris passed over and around the lens to join the fine vessels behind the lens. The lenticular capsule was completely lined with a row of epithelium. The choroid showed relatively few vessels for the eye of an infant of this age. At points where the retina was attached the choroid formed thick, vascularized mounds. The pigment epithelium of the retina was mainly atrophic. The cells were small and scantily pigmented. Occasionally the pigment cells were formed in a double layer on the choroid and were scattered in the choroid and the detached retina.

Except for six mounds of thickened choroid behind the equator, where projections of the retinal tissue were attached, the retina was detached from the optic nerve to the first ciliary process. It was collected in a stalked, atrophic mass behind the lens and iris. The roots of the projections were divided by an incomplete layer of pigment epithelium. Breaks in the epithelium allowed a few small vessels to pass. The thick central stalk was composed of connective and glial tissue, with a few thin-walled, small arteries and veins. On the temporal side the pigment epithelium of the pars plana was detached. In part it formed a border for the mass of fine connective tissue anteriorly. All evidence of organized structure of the retina was absent. The space just behind the lens was filled with fine fibrils of connective tissue. Only a few small, thin-walled vessels were seen. No hyaloid artery was visible. The cavity behind the retina was filled with exudate. Massed red cells were in the spaces behind the iris, lateral to the lens and in front of the retina. Lymphocytes and round cells were around the retinal vessels and were scattered in the retina near the hemorrhages.

A few lymphocytes were seen in the choroid and the optic nerve.

The optic nerve was atrophic. The lamina cribrosa was not fully formed.

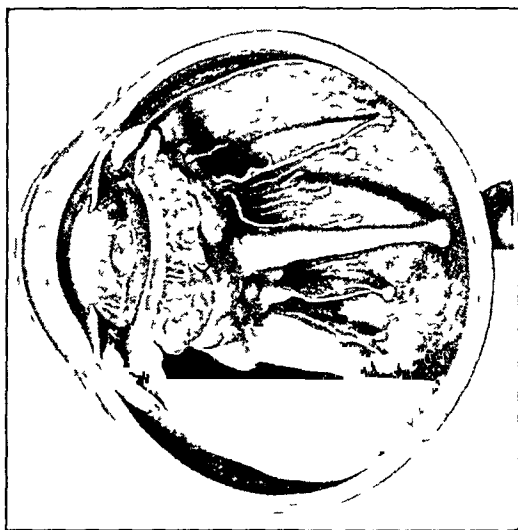


Fig. 6—Drawing of the eye from the case of Becker and Raab,<sup>7</sup> showing multiple retinal synechias after retinal detachment.

CASE 9—N. E., a white girl, was born on Nov. 20, 1939, in the University of Chicago Clinics after forty weeks' gestation, of a 29 year old primipara. She was delivered with low forceps. The placenta was normal. The Wassermann reaction of the blood was negative. The weight at birth was 3,565 Gm. The infant was placed in an incubator and given oxygen for forty-eight hours to overcome the cyanosis. At birth a hematoma, about 5 cm. in diameter, was noticed over the left occipitoparietal region. The fontanels were tense and bulging. A diagnosis of cephalohematoma, subdural hematoma, subarachnoid hemorrhage, internal obstructive hydrocephalus, secondary glaucoma (left eye) and microphthalmos (right eye) was made. The right eye was small and the left eye large. The ocular movements were not conjugate and were irregular. Both eyes tended to turn downward on illumination.

On November 22 the right eye showed a clear cornea, 8.5 mm. wide. The anterior chamber was shallow. The radial vessels of the iris were prominent and

formed a persistent pupillary membrane. The iris appeared to be close to the cornea. The pupil was round, shaggy and fixed. Its diameter was 6 mm. The pupillary reflex was gray. A grayish, irregular membranous material appeared to lie deep in the fundus. A few fine, irregular red lines on its surface seemed to be blood vessels. At 5 o'clock a narrow strip of the fundus gave a red reflex. From 10 to 1 o'clock a wrinkled, yellow mass extended down 1 to 3 mm from behind the iris on the edge of the pupil.

The cornea of the left eye was 12.5 mm wide. The anterior chamber was not as shallow as that of the right eye. A persistent pupillary membrane was not so well developed as that of the right eye. The iris was normal. The pupillary margin was even and round. The pupil was 3.5 mm in diameter and was fixed. The pupillary reflex was yellowish red. At 6 o'clock a small, irregular, fixed nodule was seen on or near the lens. The retina was poorly seen with a -20 D lens. The disk was yellowish white and larger than normal. The retinal vessels were not distinctly seen. The corneas were cloudy when the child cried.

The diagnosis was microphthalmos, secondary congenital glaucoma, retinal tumor and blindness of the right eye, and secondary congenital glaucoma, retinal atrophy and blindness of the left eye.

On March 5, 1940 the eyes were found to be relatively unchanged. The pupillary membranes were atrophied. The tension (Souter) was 12 mm in the right eye and 34 in the left eye.

In the following weeks repeated punctures of the fontanel gave a yellow fluid containing red blood cells. Examination of the blood and urine showed no abnormality. A series of roentgen treatments were given to the brain. The patient died suddenly on March 25, 1940.

An autopsy was performed by Dr. Paul E. Steiner. The diagnosis was of bilateral bronchopneumonia, aplasia of the cerebral cortex and cerebellum, agenesis of the corpus callosum and subarachnoid space, cerebral agyria, multiple heterotopias and congenital hydrocephalus.<sup>5</sup>

*Histologic Examination—Right Eye (fig 7A)* The eye weighed 3.4 Gm and measured 16.5 mm anteroposteriorly and 16 mm transversely. The cornea measured 8.5 mm in diameter and was normal. The sclera appeared normal. The anterior chamber was 1.25 mm deep. The trabeculae partly filled the filtration angle. The pupillary portion of the pigment epithelium of the iris showed minor foci of structural irregularity. Persistent remains of the embryonic vessels and mesodermal tissue of the iris passed from the iris to the anterior capsule of the lens, where it filled the pupillary space with a membrane, which was one to two cells thick. A few, fine vessels appeared on the anterior capsule. An overgrowth of the iris stroma attached to the iris projected upward behind the iris for 1.5 mm.

At points where the larger masses of membrane lay on the lens near the iris, the lens fibers were vacuolated. The posterior surface of the capsule was covered with the membrane, which had a central small pyramidal mass of cells with few capillaries. In the posterior pole of the lens the cortical fibers were disorganized, with debris, clefts and vacuoles. Several fine strands of cells pierced the capsule posteriorly and formed small nodules of proliferating cells just beneath the posterior capsule. The epithelium of the lens lined the capsule and occasionally formed more than one layer of cells. The ciliary body was small. The choroid was thin and relatively unpigmented. Only a few choroidal vessels were seen. The pigment epithelium of the retina was irregular in pigmentation and thickness. Occasionally the thin, gliosed retina was fused to the choroid. The melanotic pigment was scattered irregularly on the gliosed retina in small and large masses. The retina was about one-fourth the thickness of the normal retina. No normal cells or

stratification was present. The entire retina was a solid sheet of pigmented, gliosed tissue. Anteriorly, the retina continued as a detached retrolental membrane from a region in front of the ora serrata. It was fused to several ciliary processes. Behind the iris the membrane was composed of a mass of retinal tissue, which showed only a slight attempt at organization. The thinner portion of the membrane, behind the lens, touched the capsule and centrally was connected with a hyaloid artery, which was surrounded with a veil of mesodermal connective tissue. The hyaloid artery arose from a conical, heterogeneous mound of retinal and glial tissue on the disk. The optic disk was large and distorted, and one side was filled with unorganized retina, which showed multiple rosettes.

No evidence of vitreous fibrillae could be obtained with special stains.

A few lymphocytes, mononuclear and polymorphonuclear leukocytes were present in the uveal tract.

*Histologic Examination*—Left Eye (fig 7 B). The anteroposterior diameter was 24 mm and the transverse diameter 24 mm. The weight was 81 Gm. The

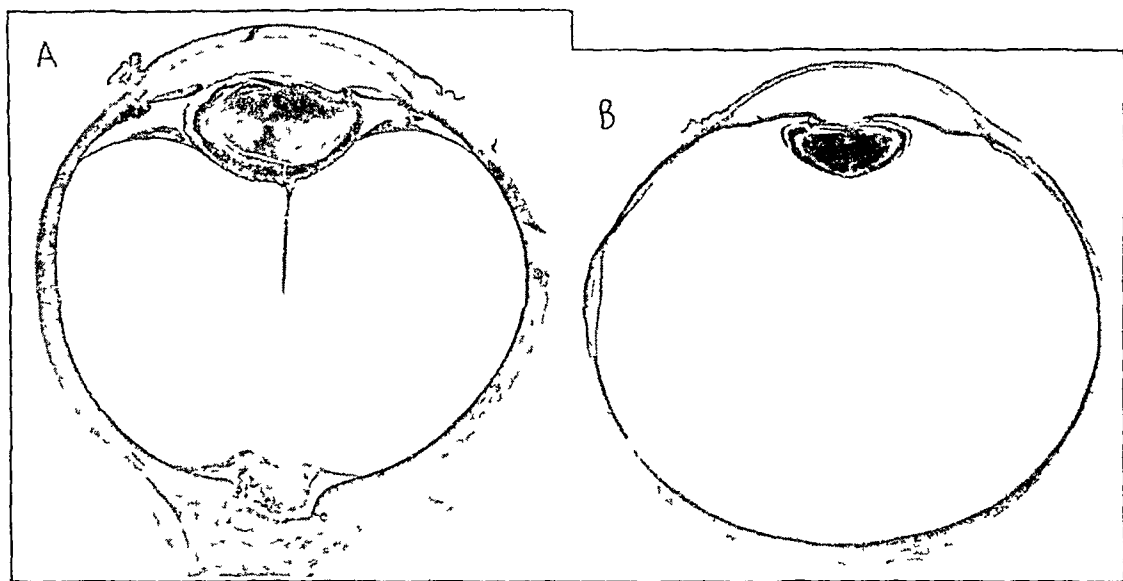


Fig 7 (case 9)—A, coloboma of the optic nerve, transverse glial membrane, persistent remains of the hyaloid artery and cataract. B, gliosis of the retina, atrophy of the choroid, iris, ciliary body and sclera, secondary glaucoma, and cataract ( $\times 45$ ).

cornea was 12.5 mm wide and was thinner and flatter than normal. The epithelium was about three cells thick in the middle. Few lymphocytes were present in the stroma. Occasional polymorphonuclear cells were on the posterior surface of the cornea. The canal of Schlemm was small and was absent in some sections. The anterior chamber was 2 mm deep. The sclera was about one-half normal thickness. The iris and the ciliary body were atrophic. The thin, flat ciliary processes were far forward, one half on the ciliary portion and one half on the posterior surface of the iris. A few round cells and lymphocytes were present. The pupillary border of the iris was adherent to the lens capsule, and in places the pigmentation of the iris covered the pupillary area. The lens was flatter than usual. The posterior pole showed slight vacuolation. A small nodule of epithelial cells was beneath the posterior capsule.

The choroid was thin and its vascularity not prominent. A small segment of the retina extended forward to the root of the iris, where they formed a fold. The extensions were thicker and more stratified and organized than the rest of the retina. The retinal pigment epithelial cells were irregular in size. The pigment granules were scattered among the outer members of the bacillary layer. The nuclei of the outer nuclear layer of the retina were oval or long, and the cells

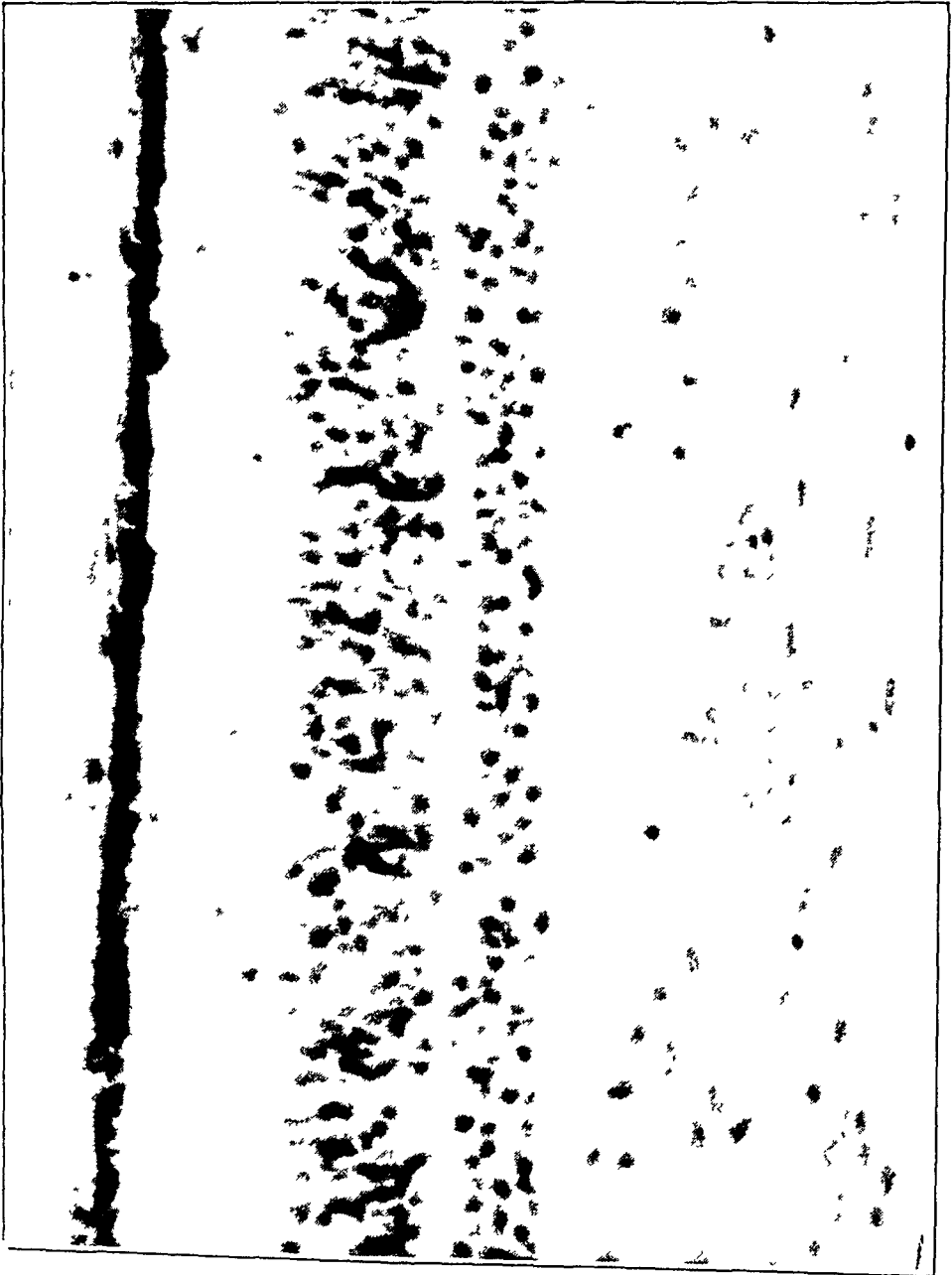


Fig 8 (case 9) —Marked retinal atrophy and gliosis of the left eye

showed filamentous processes. The outer limiting membrane was absent in the conspicuously unorganized outer nuclear layer. The outer reticular layer was slightly thinner than normal. The outer nuclear layer was thin, irregular and two to five cells deep (fig 8). The inner reticular layer was thin or absent. The nerve fiber layer was heavily gliosed. Occasionally lymphocytes and mononuclear cells were seen on the surface of the retina. The surface of the papilla was gliosed. The



columns of nerve fibers in the optic nerve were irregular as a result of gliosis. A few leukocytes were noted.

CASE 10—R L, a white girl, was born in the University of Chicago Clinics in good condition without the aid of instruments on Aug 4, 1938, at the full term of a second pregnancy. The placenta was normal. The weight at birth was 2,770 Gm. There was no evidence of hemorrhage, jaundice or cyanosis.

The father, aged 31, the mother, aged 30, and the sister, aged 3½ years, were healthy. There was no history of ocular or nervous disease in the family. There had been no previous abortions or miscarriages. The mother sprained her ankle in an automobile accident during her fifth month of pregnancy.

The infant was brought to the University Clinics for pediatric examination on Nov 4, 1938. In October 1938 the infant had begun to have major convulsions several times a day. The convulsions were recurrent until Sept 14, 1939, when the patient was last seen. The child was well developed physically, although obese, but mentally she was remarkably retarded. A macular, pigmented nevus, 4 cm in diameter, was present on the right thigh. Neurologically, except for the eyes, a small head and the occurrence of convulsions, the patient was not abnormal. Roentgenographic examination of the skull suggested no cause for the convulsions.

The left upper eyelid was lower than the right. The pupils were equal in size. The right pupil reacted slowly, and the left was fixed. The external ocular movements suggested slight weakness of the left internal rectus muscle. A diagnosis of microcephaly and cerebral agenesis was made.

On Jan 12, 1939 examination of the patient's eyes revealed a flat, gray mass in the right fundus, which had not been seen two months previously. The mother had observed nothing unusual about the eyes or vision. On January 13 the eyes were examined while the child was under ether anesthesia. The right palpebral fissure was slightly larger than the left. The external ocular movements were normal. The conjunctivas and corneas were clear. The irises were normal. The pupils were round and regular. The right pupil reacted slowly to light, and the left was fixed. The media were clear.

The right fundus was best seen with a -6 D lens. Just above and below the pale disk along the superior and inferior nasal vessels were two gray-white plaques, about 2 disk diameters wide, which were sharply defined and slightly elevated. The retinal vessels passed over these lesions without change of direction. Five other small white, flat retinal lesions were on the temporal side next to the disk. The margins of the disk were blurred.

The left fundus was best seen with a -4 D lens. The lesions measured about 1 disk diameter and lay close to the disk. A yellow-white plaque was just above and another was below the disk. The third spot was above and nasal to the margin of the disk. A tentative diagnosis of bilateral retinoblastoma was made.

On March 31, 1939 a reexamination of the fundi was made. The lesions were slightly larger and hazier in appearance than previously.

The right eye was removed on April 4, 1939. High voltage roentgen therapy was given to the whole skull and to the left eye. For a period of three months the lesions of the left fundus were constant in size, but later they became slightly larger. The blood cell count and urine were normal. The Wassermann and intradermal tuberculin tests gave negative reactions.

On Nov 12, 1939, when the patient was admitted to a state institution, she had a chronologic age of 1 year 3 months and an intelligence quotient of 5. On Dec 10, 1939 she had diphtheria, from which she recovered. On Jan 31, 1940 she died of bronchopneumonia.

By permission of Dr B W Lichtenstein, the neurohistologist, a brief report of the autopsy is given for comparison with that of Walker<sup>5</sup>

"Postmortem examination revealed an advanced bronchopneumonic process, involving both lobes of the left lung and the base of the right, congestion of the liver, conspicuous congestion of some of the larger vessels of the brain, and gelatinous substance in the cerebellum

"The brain weighed 576 Gm without the dura It was small, and the leptomeninges over the frontal lobes were thickened The cortical gyri were irregular in size and shape Some in the frontal lobes were large Large and undular masses were present in some gyri in the frontal lobes Other gyri were divided by tiny sulci, giving rise to microgyria The parietal and occipital lobes were smaller than the frontal lobes The arachnoid over the interpeduncular space was thickened The first cranial nerves were absent The optic nerves were small A large cyst with a smooth wall was present in the right lobe of the cerebellum The corpus callosum was absent except for two folds extending along the medial border of the lateral ventricles There was no septum pellucidum The walls of the lateral ventricles were studded with many irregular nodules The third ventricle was greatly dilated Heterotopic gray masses were disseminated throughout the cortex, internal capsule and caudate nucleus The islands of Reil were irregular and cut by many shallow sulci No mamillary bodies were seen in the section taken behind the tuber cinereum The cornu ammonis was hardly recognizable A large depression occurred in the right occipital lobe A large heterotopic mass was seen in the right hemisphere of the cerebellum

"Staining revealed massive and numerous heterotopias, composed of ganglionic cells, for the most part, which were small and were not well supplied with Nissl substance, and glia, which consisted of both astrocytes and oligodendrocytes The cortex was normal except where the heterotopias disturbed the usual structure

"The cerebellar cyst was a simple cavity without a distinctive lining

"In the medulla the pyramidal tracts were small and the fibers scanty

"The diagnosis was (1) bronchopneumonia, with congestion and toxic changes in other viscera, (2) cerebral agenesis with heterotopias, involving (a) absence of the olfactory bulbs and nerves, (b) absence of the corpus callosum, (c) absence of the mamillary bodies and (d) microgyria, and (3) simple cyst of the right lobe of the cerebellum"

*Histologic Examination*—Right Eye The anteroposterior diameter of the eye was 19 mm The cornea was 10 mm in diameter The anterior chamber was shallow The canal of Schlemm was small and was not visible in every section The pigment layer of the iris at the pupillary margin was adherent to the lens capsule The choroid, ciliary body and lens were normal The sclera was slightly thinner than normal

The retina (fig 9) corresponding to the several small areas of atrophy, as seen through the ophthalmoscope, showed unpigmented pigment epithelium The cells of this layer were slightly larger than normal The large lesions just above and below the disk were apparently formed by areas of lightly pigmented pigment epithelium Nasal and temporal to the disk were two flat lesions, about 2 to 3 mm in diameter The temporal lesion showed multiple large microcysts in the inner and outer reticular layers and in the inner nuclear layer Below the large fused microcysts of the retina the pigment epithelium was unpigmented In the nasal lesion the cystic spaces opened into the subretinal fluid under an unattached retina The subretinal cavity was evenly lined outwardly with unpigmented retinal epithelium In the deepest part of the cyst, which was about 100 microns deep,

several pigmented and unpigmented epithelial cysts were seen in the subretinal fluid. The nasal side of the lesion showed a small fold of pigment epithelium overlying the subretinal cavity.

Temporally, an area 27 mm in diameter, extending forward to within 15 mm of the ora serrata, showed an irregular nerve fiber layer. Multiple short fibers extended from the nerve fiber layer into the vitreous. The greatest thickness of this layer was 16 mm. Near the ora serrata the bacillary layer of the retina



Fig 9 (case 10) —Posterior part of the right eye near the disk

was unevenly attached to the pigment epithelium and was distorted. A small narrow projection of unorganized retinal cells ran forward over the pigment epithelium as far as the ciliary processes.

The optic nerve was normal.

CASE 11—J. Z., a white boy, was brought to the University of Chicago Clinics for an ophthalmic consultation on Jan 20, 1944.

He was born in another hospital on Dec 1, 1942, after seven months' gestation, with a weight of 1,360 Gm. No instruments were used in the delivery. The cause of prematurity was unknown. The child was placed in an incubator for twelve weeks. In the fifth month of pregnancy the mother had a bloody vaginal discharge for one day. During the sixth month she received intravenous injections of a "yellow fluid" three times a week, in spite of a negative reaction of the blood for syphilis. The mother believed that the father had a venereal infection, although his blood gave a negative serologic reaction. The father, aged 27 years, the mother, aged 27 years, two brothers, aged 4 and 5 years, a sister, aged 3 years, and other relatives were well and had no obvious ocular or nervous disease. No evidence was obtained by inquiry of the presence of virus diseases in the family during the first months of pregnancy.

When the child arrived home, at the age of 3 months, the mother noticed that the eyes behaved differently from those of other children and that they followed only bright lights. She was told by the obstetrician that the child was blind at birth. In another clinic, on May 21, 1943, a diagnosis of bilateral persistent tunica vesiculosa lentis was made. As a result of examination, on June 6, bilateral retinoblastoma was suspected, and an operation was advised.

On Jan 21, 1944 the child was examined in this clinic. A diagnosis of severe emaciation, hypochromic anemia and mental retardation was made. The child weighed 5,320 Gm. The circumference of the head was 41.5 cm. Roentgenologic examination of the skull showed no abnormalities. Agglutination tests with brucella, *Pasteurella tularensis*, and *Proteus vulgaris* OX19 gave negative results. The Kahn reaction of the blood was negative. The urine was normal. The red blood cell count was 3,800,000 and the hemoglobin was 3.8 Gm per hundred cubic centimeters. The anemia was later cured by medication.

The head turned toward light, but the conjugate movements of the eyes were inconstant. Light perception was present, but there was no fixation. The corneas were 7 mm in diameter. The pupils, 2 to 3 mm in diameter, reacted slowly to light. The anterior chambers and irises appeared normal. The pupils did not give a red reflex. Gray, nonvascular masses lay behind each pupil, close to the lens. The retina of the right eye was given 700 r and the retina of the left eye 350 r.

On Feb 17, 1944 another ophthalmic examination was made. Central visual fixation was not sustained. Externally the eyes were normal. The corneas were 7 mm in diameter. The anterior chambers were shallow. The markings of the iris were blurred. The right pupil was 3 mm, and the left 2 mm in diameter. With dilation with atropine the right pupil was 5 mm, and the left 3 mm, in diameter. Incomplete posterior synechias produced irregular pupils. A thin veil passed over the anterior surface of each lens. Posteriorly, close to each lens was an irregular, gray mass with peripheral vessels. The light reflex was a dull gray. Dentate processes were seen at the extreme periphery of the fundus of each eye. The tactile tension was normal. Dr. T. L. Terry, of Boston, made the diagnosis of retrolental fibroplasia.

On Aug 8, 1944 the corneas measured 10 mm in diameter. The left cornea was slightly hazy. The anterior chambers were almost collapsed. The right pupil measured 3 mm and was round. The left pupil was ragged. Both pupils were bound by posterior synechias. The retina of the right eye was seen as a smooth gray mass, touching the lens. No retinal or iridic vessels were seen. The left eye showed an opaque lens. No vision or reaction to light was obtainable. Tactile tension seemed to be increased.

The child was malnourished, poorly developed and mentally retarded. On Nov 27, 1944 the intelligence quotient on the Kuhlmann scale was 37.

A diagnosis of bilateral microphthalmos, congenital detached retina, anterior and posterior synechias and complicated cataract was made.

CASE 12—C D, a white boy, was born July 23, 1941 in the University of Chicago Clinics after thirty weeks' gestation. The weight at birth was 1,745 Gm. Delivery was by cesarean section, after the mother had had a uterine hemorrhage. The placenta was normal. The cause of the prematurity was unknown. At birth respiration was delayed two minutes, and the cyanosis was moderate and transitory. There was no jaundice. The infant was kept in an incubator until August 22, when he was discharged from the hospital in a healthy condition with a weight of 2,505 Gm.

The father, aged 31, the mother, aged 28, a brother, aged 8 years, and three sisters, aged 6, 4 and 2 years, were well. The siblings were born after full term pregnancies and with normal deliveries. The second pregnancy terminated in six months with induced delivery after uterine hemorrhage. The premature infant, who was normal, died in seventeen minutes. The mother's sister had questionable tuberculous lymphadenitis, and the maternal grandmother was partly blind. No other member of the family had any ocular disease, and there was no history of nervous disease in the family. The mother's parents were cousins.

When the patient was 9 months old, he was treated for spasms by the family doctor, who noticed that the child was blind. The mother had been advised by two ophthalmologists that the child had pseudogliomas.

On Dec 12, 1943 examination showed that the child was blind and mentally retarded. Gray masses, suggesting pseudogliomas, were seen back of each pupil. Examination of the blood showed mild anemia, and the spinal fluid was normal. The mother refused to permit further examinations.

On May 4, 1944 an ophthalmic examination was made. The child, according to his mother, was apparently blind in September 1941. The eyes did not follow light or blink on exposure to bright light. The eyes seemed small for the head. The right cornea was clear and measured 10.5 mm in diameter. The anterior chamber was shallow. The pupil was 5 mm in diameter and was bound down with posterior synechias. No pupillary membranes or vessels were seen. The posterior surface of the lens was completely covered with a gray, nonvascular mass except at the extreme periphery, where a red reflex was obtained. The left cornea was 10.5 mm in diameter. The anterior chamber and iris appeared normal. The pupil reacted to light. No pupillary membranes or vessels were seen. A gray mass filled the upper half of the left fundus behind the lens. A grayish stalk, 2 mm in diameter, containing blood vessels, extended back to a pale gray area of 1 papilla diameter, corresponding to the disk. Dark granular and clumped pigment was scattered throughout the rest of the fundus, which was reddish. No retinal vessels were visible. The choroidal vessels were fairly well seen.

A diagnosis was made of retrolental fibroplasia of both eyes and postinflammatory chorioretinitis of the left eye. Because of the blindness and cerebral agenesis with mental retardation, the child was committed to a state hospital in June 1944. He was still living on Aug 11, 1944.

CASE 13—J K, a white girl, was born Aug 20, 1939 in an outside hospital after seven months' gestation. The weight at birth was 810 Gm. The second infant of the twins, born after J K, died after five hours. For the first twenty-three days the child was treated with oxygen. She was kept in an incubator for one hundred days. Her weight was then 2,670 Gm.

The father, aged 37, and a sister, aged 6 years, had hereditary supernumerary toes. The mother, aged 36, showed persistent high blood pressure. Her mother at the age of 46 had a cerebral tumor. A sister of the infant's mother was obese. Sisters of the patient, aged 4 and 11 years, were normal. The family gave no evidence of mental retardation or signs of hereditary ocular diseases.

In May 1940 the mother observed that the right eye protruded. She was told by a physician that the child had cataracts. The blindness was noticed when the child was 3 months old.

On Jan 13, 1941 the mother brought the child to the hospital for advice about blindness and lack of physical development. After an examination, a diagnosis of bilateral supernumerary toes, right hemiparesis and cerebral agenesis was made. The blood count and the urine were normal. The Wassermann reaction of the blood was negative. The supernumerary toes were removed surgically.

The child was photophobic. No sense of light projection was evident. The external ocular movements were normal. The left eye was enophthalmic. The eyes were equal in size. The right eye showed a central corneal nebula. The anterior chamber was shallow. The pupil, 3.5 mm in diameter, was fixed by posterior synchias. The lens was densely opaque. No fundus reflex was obtainable.

The left eye showed a clear cornea and lens. The anterior chamber was shallow. The pupil was 4 mm in diameter, but it was not reactive to light. With homatropine the pupil dilated to 7 mm. The retina was green-gray and was detached as far as the ora serrata. It floated forward in the form of a funnel, obscuring the disk. The large retinal vessels ran posteriorly toward the hidden disk until they were hidden by the folds of the retina. No hemorrhage or tumor was noted.

On April 7, 1941, an attempt to extract the cataract of the right eye was unsuccessful because the lens was hard and opacity of the cornea interfered with observation of operation.

The patient was last seen Oct 15, 1941. The condition of the eyes was unchanged.

CASE 14—J. S., a white girl, was born in the University of Chicago Clinics on June 2, 1937 after thirty-eight weeks' gestation. The placenta was normal. The weight at birth was 3,410 Gm. There was no postnatal cyanosis or jaundice. The child was normal except for the eyes, which were small and were kept closed. There was no sign of vision.

The mother, aged 18, a primipara, had had preeclamptic toxemia of pregnancy. The father, aged 25, was well. The parents knew of no familial disease.

The eyes were examined on June 15 in the University Clinics at the request of the obstetrician. The bulbs were smaller than normal and were deeply set in the orbits. The lids were kept partly closed. The eyes gave no reaction to light. They converged slightly, but the external ocular movements were unrestricted.

The right cornea was 6 mm, and the left 7 mm, in diameter. The anterior chambers were apparently of normal depth. The right cornea was slightly cloudy. Tactile tension could not be taken. The pupils were irregular and fixed to light. Behind the lens, a greenish gray mass was seen deep in the fundus of each eye. The mass was larger in the right eye than in the left. A diagnosis of bilateral glioma was made. Dr. Sanford Gifford, in consultation, examined the eyes on July 8 and expressed the belief that the child had microphakia, and not glioma.

On August 20 the corneas were seen to be clear, and the gray mass in each eye was close to the posterior surface of the lens. The child was repeatedly observed by pediatricians, neurologists and ophthalmologists.

Since the age of 1 month the head had steadily increased in size. On Aug 30, 1937 the circumference of the head was 49 cm. A trephination showed that the cortex was thin and was lying close to the dura mater. A cloudy, yellow fluid was obtained from the ventricles. A diagnosis of hydrocephalus secondary to obstruction of the ventricular system was made.

Ophthalmic examination, on April 6, 1938, showed that the eyes were unchanged in size. The corneas were clear. The anterior chambers were not shallow. The lenses were cataractous. A diagnosis of bilateral pseudoglioma and cataract was made. On June 2, 1938 the head was 71 cm in circumference, and the fontanelles were wide and tense. Signs of meningeal irritation were present. There was no history of vomiting or convulsions.

The patient was last seen on Sept 24, 1938. The condition of the eyes was unchanged. On Sept 25, 1938 she was admitted to another hospital, where she died, March 5, 1939.

The diagnosis obtained from the autopsy record was congenital hydrocephalus, cerebral edema and pneumonia. No retinal glioma was observed.

CASE 15—D. H., a white girl, was born May 3, 1942 in the University of Chicago Clinics after a gestation of thirty-one weeks. The cause of the prematurity was unknown. After delivery respiration was delayed for two minutes. The weight at birth was 1,580 Gm. The child was placed in an incubator for twenty-six days and was discharged from the hospital at the age of 47 days. The weight then was 2,500 Gm. There was no history of cyanosis or jaundice.

The father, aged 40, the mother, aged 38, the brothers, aged 10 and 12 years, and the sisters, aged 16 and 20 years, were well. The family had no history of nervous or ocular diseases.

On August 8 the mother brought the child to the University Clinics for treatment of constipation. She had noticed no abnormalities of the eyes. Physical examination revealed for the first time a small, yellowish gray mass on the nasal side of the right fundus. A smaller gray mass was seen in the left fundus. The child was otherwise healthy. The weight was 4,200 Gm. Roentgenographic examination of the skull and optic foramina revealed nothing abnormal. The blood and urine were normal.

On Aug 11, 1942 the eyes were examined again. Vision was nil. The anterior chamber of the right eye was obliterated. The iris pattern was blurred, but atrophy was not present. Anterior synechias were present. Posterior synechias were seen except at 3, 6, 9 and 12 o'clock where the pupillary reflex was dark. The pupil measured 3 mm in diameter and was fixed and elliptic. A yellowish gray mass behind the lens filled the middle of the pupillary space. It was traversed by small vessels arising from the superior nasal and temporal quadrants. The mass was high in the center and was distinctly seen, but peripherally it appeared blurred.

The changes of the left eye were similar to those of the right eye. The anterior chamber was obliterated. Complete anterior and posterior synechias were present. The iris was not atrophic. The pupil was round and fixed. A yellowish gray mass filled the space behind the lens and gave a gray pupillary reflex. The mass showed a wavy surface, which was darkened in spots with pigment. Small retinal vessels from the four quarters of the fundus passed over the mass. The central mass in each eye was best seen with a +20 D lens. A diagnosis of probable bilateral detachment of the retina was made.

In another clinic, on April 23, 1943, the eyes were found to show little change. The infant was mentally retarded.

CASE 16—R F, a white boy, was brought to the University of Chicago Clinics on April 10, 1941 by the mother, who said that the child had never been able to sit up, to hold his head up, to walk or to talk. He was born in another hospital on Feb 4, 1938 after seven months' gestation. The cause of the prematurity was unknown. The weight at birth was 1,770 Gm. The infant was kept in an oxygen tent for three weeks and was discharged from the hospital after five months. The child had always been blind. His eyes were never fixed on his parents or on moving objects. Objects were not grasped unless they were placed in his hands. He had never had convulsions and had never been injured.

The father, aged 30, the mother, aged 26, the brothers, aged 4 and 6 years, and a sister, aged 1 year, were well. The parents knew of no nervous or ocular disease in the relatives or ancestors.

*Physical Examination*—The child was small and weak. The weight was 102 Kg. The urine was normal. The red blood cell count was 5,150,000, and the hemoglobin content was 8 Gm per hundred cubic centimeters. The Wassermann reaction of the spinal fluid was negative. Roentgenographic examination showed a normal skull. Vision was nil. The bulbs and corneas were normal in size. The anterior chambers, irises and lenses appeared to be normal. The pupils gave no reaction to light. With atropine they dilated to 4.5 mm. In the right eye a gray mass of detached retina, traversed by retinal blood vessels, was seen to extend from the temporal side of the disk to the periphery. The mass was best seen with a +7 D lens. On the nasal border of the mass a yellow-gray area, 1 disk diameter in width, ran vertically over the disk. The nasal half of the fundus was pale, flat and indistinct. It was best seen with a +2 D lens. The left fundus was similar to the right. A central gray mass, which was best seen with a +8 D lens, covered the disk and the macula. It arose from the retina in sharp vertical ridges. The retina laterally and superiorly was pale, indistinct and slightly elevated. The tension (Schiotz) was 19 mm of mercury in the right eye and 21 mm in the left eye.

A diagnosis of spastic quadriplegia, cerebral agenesis and bilateral congenital detachment of the retina was made.

CASE 17—B B, the first of identical white female triplets, was born without difficulty on Jan 30, 1943 in the University of Chicago Clinics after twenty-nine weeks' gestation.

The second triplet was normal at birth but died at the age of 4 months of pneumonia. The third triplet was previsible and died thirty hours after birth. Postmortem examination of the third triplet was performed by Dr Edith Potter. The child weighed 920 Gm and was 37 cm long. The pathologic diagnosis was viability, constriction rings on the proximal phalanx of the first and fifth toes, fusion of the third and fourth toes of the left foot, and amputation of the first four digits of the right foot from amniotic bands, atelectasis, and collapse of the alveoli. The brain and other organs were normal.

The single placenta, weighing 756 Gm, had three cords attached marginally at equal distances. There were three amniotic sacs and a single chorion.

The father, aged 28, the mother, aged 27, a sister, aged 3 years, and the grandparents and great-grandparents were well. There was no history of nervous or ocular disease in the family or ancestors. The mother had measles when she was a child. The Wassermann reaction of the mother's blood was negative.



The patient weighed 1,085 Gm on the fourteenth day of life. She was kept in an incubator and was discharged from the hospital in sixty-four days. For the first ten days in the hospital she was jaundiced. At the age of 105 days she had pertussis for six weeks. In April roentgen therapy was given to a cavernous hemangioma, 3 cm in diameter, on the chest.

On June 15, 1943 the patient was taken to the University Clinics for a routine examination. The mother had noticed no defects in the eyes or vision of the infant. Examination showed a premature child in good health, with a weight of 5,220 Gm. The child was normal except for a white mass behind the lens on the nasal side of the fundus of the left eye. A diagnosis of pseudoglioma of the left eye was made by a pediatrician.

On July 8 it was noted that the eyes followed light but not objects. Occasionally the eyes showed a tendency to convergent squint. The corneas and irises were normal. The pupils were reactive to light. The nonvascular, white opacities seemed to be in or next to the lens. The fundus reflex was red. The skull and optic foramina appeared normal in roentgenograms.

Reexamination of the eyes on Sept. 14, 1944 showed searching movements and occasionally a convergent squint. The right eye followed blocks 1 inch (2.5 cm) square, held close to the eyes. Vision of the left eye was apparently limited to light perception only. The corneas were 10 mm in diameter. The anterior chambers were shallow. The irises seemed normal. The right pupil was more reactive to light than the left, the pupil dilated to 8 mm with atropine. The right lens was clear. The left lens was clear except for a few irregular, translucent radial striae. Just behind the right lens, from 3 to 5 o'clock and 5 mm from the center, was a nonvascular, smooth-surfaced, gray mass. Peripherally, behind the iris, the multiple radial, black and white ciliary processes joined the mass, which extended laterally and backward as a broad-based stalk, fused to the nasal side of the fundus and to the invisible optic disk. No vessels were seen on the stalk or the retina. Several crescents of dark granular pigment were around the site of fusion of gray tissue to the posterior pole of the fundus. The fundus was best seen with a -25 D lens as a diffuse red reflex without vascularity.

The mass behind the left lens was seen nasally 2 mm from the center. It covered the posterior surface of the lens from 7 to 12 o'clock and extended nasally as a winged, broad-based stalk to the area of the disk. Few floating pigment granules were observed in the postlental space. No vessels were seen. The nonvascular, red surface of the fundus was best seen at -25 D. The intraocular tension (Souter) was 10 mm in the right eye and 16 mm in the left eye.

Psychometric tests indicated that the child was retarded mentally by blindness and by the excessive protection and care of the mother.

A diagnosis of bilateral congenital retinal fold was made.

CASE 18—B. W., a white boy, was born in Chicago Lying-In Hospital on Jan. 12, 1944 after thirty weeks' gestation. The weight of the infant was 1,150 Gm and the length was 36 cm. Because of the loss of amniotic fluid twelve days previously, abruptio placentae was suspected, and birth was induced with artificial rupture of the membranes. No instruments were used in the delivery. The newborn infant showed no signs of cyanosis, jaundice or hemorrhage. The Kahn reaction of the mother's blood was negative. The father, aged 23, and the mother, aged 17, were well. The child was the result of a first pregnancy. There was no history of ocular or nervous disease in the family or the ancestors.

The infant was given vitamin K and placed in a Hess bed with a constant supply of oxygen. The child was healthy during his stay in the hospital except for persistent nonpitting edema of the legs. On discharge, at the age of 65 days,

he weighed 2,540 Gm, the hemoglobin content was 10 Gm per hundred cubic centimeters, and the red blood cell count was 3,100,000. The eyes appeared normal.

The condition of the infant's health was followed at a welfare station. On Sept 26, 1944, by request, the child came to the University Clinics for examination. He was not gaining weight well. The mother observed that the infant had not been able to fix his eyes on objects for the past three months. Examination showed a small child, weighing 6,100 Gm, who was underdeveloped physically. His length was 62 cm, and the circumference of his head measured 41 cm. He was unable to sit up alone but was able to roll to one side. His blood picture was that of hypochromic anemia. Roentgenographic examination revealed a marked retardation of bone development in the extremities. A psychometric test indicated pronounced mental retardation not related to poor vision or prematurity. The pediatrician noticed a retrolental mass bilaterally. A diagnosis of immaturity, nutritional anemia, cerebral spastic palsy, bilateral retrolental fibroplasia and mental retardation was made.

On September 27 the eyes were examined. There was no response to light. Externally the eyes were normal. The corneas were clear and measured 10 mm in diameter. The anterior chambers were shallow. Anterior and posterior synechias were present. The pupils, 3 mm in diameter, were irregular and fixed. Atropine and neo-synephrine produced slight dilatation. The lenses were clear. In the right eye behind the lens was a pink-gray mass, which was wrinkled like parchment. Radial vessels of the same caliber as normal retinal vessels were seen in the center of the mass. No details were noticed in the peripheral indistinct orange reflex. In the left eye a pink-gray avascular mass was seen just behind the lens. Nasally and peripherally a blurred, indistinct orange reflex was obtained.

A diagnosis of bilateral congenital detachment of the retina was made.

The patient was last seen on Oct 25, 1944. The physical condition was unchanged.

#### PATHOLOGIC FEATURES

A total of 16 eyes were removed surgically, because of blindness with intolerable pain or a presumptive diagnosis of retinoblastoma, or at autopsy. The eyes were fixed in Held's solution, embedded by means of the slow pyroxylin method and sectioned serially. Various appropriate staining methods were employed to show histologic structures and processes.

*Microphthalmos*—The presence of microphthalmos in the first few months of life of a premature infant is difficult to determine. An eye may be abnormally small at birth because of prematurity, congenital microphthalmos or arrested growth due to detached retina or other pathologic process. Furthermore, a microphthalmic eye may have a secondary glaucoma, which increases the size of the eye but not its structural parts.

Of the 9 microphthalmic eyes, 7 had a totally detached retina, which in most instances was relatively well atrophied. The clinical secondary glaucoma in 3 of these eyes was either of too short duration or too transitory to effect the size of the eye. The full term infant with microphthalmos had a long-standing retinal detachment and retinal synechias at birth, with no signs that intrauterine glaucoma had affected the size

The detachment of the retina may hinder the growth of the bulb, but the evidence was not remarkable in these infants with a gestational age of 7 months or less. Two of the 9 microphthalmic eyes had no retinal detachment. One showed general retinal dysplasia, and the other, general retinal gliosis, atrophy and glial hyperplasia of the anterior part of the retina and persistent hyaloid artery. A large eye with gliosis of the retina, which was not included with the 9 microphthalmic eyes, was microphthalmic in structure but became large probably as the result of secondary early fetal glaucoma of long duration.

*Cornea*—The diameter of the cornea varied with the gestational and the living age and with the amount of intraocular pressure. The diameter of the microphthalmic eyes was generally within the lower limit for the normal eye of the corresponding total (i. e., living and gestational) anatomic age.

Glaucoma after a retinal detachment of long duration, which was indicated by almost complete atrophy of the retina, produced a bulb of average size or slightly larger, a thin sclera and choroid and a large cornea in an eye with partly arrested growth. Congenital glaucoma in an eye with complete retinal gliosis resulted in a greatly enlarged bulb with a thin sclera and a thin cornea of abnormally large diameter. It seemed that a glaucoma lasting several months enlarged the bulb, stretched the sclera and widened and thinned the cornea during the late prenatal or early neonatal period.

*Anterior Chamber*—The anterior chamber was of normal depth in the eyes with the iris beginning to adhere to the lenticular capsule. After complete posterior synechias formed and a heavy exudate occurred in the intraretinal space, the anterior chamber became shallow. The chamber was almost totally collapsed after exudate and hemorrhage entered the space posterior to the iris. In some eyes the iris and the lens were pushed forward into the space of the anterior chamber. In most of the eyes the filtration angle was immaturely developed and the canal of Schlemm was partly covered. The effect of age, prematurity and arrested growth on the immaturity of development of the trabeculae and the filtration angle is difficult to determine. In some eyes the filtration angle was closed in various degrees by the adherence of the periphery of the iris to the cornea as a secondary effect. In 1 eye central anterior synechias were present. The anterior synechias were a part of the process that followed the detachment of the retina.

*Iris*—In eyes without retinal detachment there was a tendency for the iris to agglutinate, and later to adhere, to the lenticular capsule. In the eyes with pronounced inactive gliosis of the retina the posterior synechias probably indicated only part of a disease process of long duration before birth. Apparently, after the retinal detachment the

iris became engorged and then edematous. Later, cysts of iridic pigment epithelium formed in some eyes. Proliferation and extension of new strands of connective tissue and fine capillaries from the adjacent anterior layer of the iris onto the lenticular capsule occurred in several eyes. Since early clinical examination of the pupillary area revealed no traces of these vessels or connective tissue strands, they were not vestigial remains of a fetal vascular system. In 2 eyes the new strands passed through the pupillary area toward the equator of the lens and terminated there. In an eye with a collapsed anterior chamber and with central and peripheral anterior synechias, proliferation of connective tissue, pigmented cells and capillaries occurred in the pupillary space.

*Ciliary Body*—The ciliary body and iris became atrophic during the persistent glaucoma. In the eyes with fetal glaucoma the ciliary processes were atrophic, but in the eyes with glaucoma occurring after retinal detachment the cellular reaction varied seemingly with the degree of intraocular pressure and the amount of intraretinal and postiridic exudate and hemorrhage. A low intraocular pressure and the presence of exudate with much protein tended to produce more proliferative response from the ciliary epithelium, neuroglia and connective tissue cells. As a result, a lamellar hyaline and connective tissue membrane formed to a greater or less degree behind the lens and extended transversely over the anterior limits of the detached retina.

*Sclera*—The sclera was stretched thin in eyes with long-standing glaucoma. The lamina cribrosa was only slightly deflected outwardly, if at all.

*Choroid*—The choroid was immature in development in the younger premature infants. Frequently the choroid was engorged after retinal detachment if the cellular reaction of the anterior uveal tract was intense. Very heavy exudation in the intraretinal space was usually accompanied with separation of the anterior epichoroidal lamellas by a serofibrinous exudate.

Prolonged glaucoma produced atrophy of the choroid. In the eyes with the gliosed retina the atrophic choroid was fused to the retina. In the one eye of the full term, 1 day old infant born with a bilateral detached retina the retina was reattached in six places. The retinal synechias were identical in appearance with those shown by Becker and Raab<sup>7</sup> in the picture of primary retinal detachment (fig 7). The choroid was hypertrophied and well vascularized at the junction with the retinal synechias. That this process occurred in fetal life is obvious, as the

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<sup>7</sup> Graefe, A., and Saemisch, T. Handbuch der gesamten Augenheilkunde, Leipzig, Wilhelm Engelmann, 1916, pt 2, chap 10a, no 2, pp 1453 and 1560.

infant died during the first day of life. In the eyes with dysplastic retinas the choroid was relatively hypoplastic.

*Retina*—The retina was the tissue commonly affected in eyes with congenital encephalo-ophthalmic dysplasia. The retina in the sections of 2 eyes was dysplastic. The nerve elements were hypoplastic, and the supporting nerve tissue was hyperplastic. An abnormal, unorganized overgrowth of retina at the ora serrata, agenesis of melanotic pigment in the pigment epithelium of the retina, glial hyperplasia of the retina, hypoplasia of the nuclear layers and a coloboma of the pigment epithelial layer of the retina occurred. In both eyes one or more small serous separations of the retina between the pigment epithelium and the bacillary layer were evident. There is a good possibility that the retinal detachment began locally with a choroidal effusion. It could explain the small pigmented lesion after retinal atrophy which Terry described in the eye of 1 of his patients, as well as the lesions in these 2 eyes.

In 2 eyes the anterior part of the retina was overgrown and formed a transverse postlental membrane after atrophy and gliosis.

Complete detachment of the retina was found in 12 eyes. The retina was usually massed forward behind the lens and the iris. If detachment happened early before birth, the stalklike base was a glial shaft of nerve fibers extending to the atrophic retina. No definite, large hyaloid artery could be seen. In a few eyes part of the retina was a fused mass at one side. The remainder of the retina was detached, like a sac, which was displaced anteriorly. The retinal mass in some instances was extremely atrophic. The nerve cells were almost entirely absorbed, and only large glial and small connective tissue strands remained. This late atrophy of the retina explained the increasing redness of the pupillary reflex as the disease progressed in some eyes.

It is possible that the retinal atrophy followed the flat detachment produced by the serous effusion in the first 2 eyes, if this is true, the process of gliosis of the retina in the other 2 eyes would be similarly explained.

*Optic Nerve*—The optic nerve in the eyes of the infants over 2 months of age was almost completely medullated. The optic nerves in the eyes with a totally gliosed retina could not be examined properly. In the eyes with fetal detachment of the retina, with pronounced retinal hypoplasia and with detachment of long duration the number of nerve fibers seemed to be less than normal. In 2 eyes the nerve head showed malformations.

*Lens*—The lenses in eyes with a detached retina showed no abnormalities except for proliferation of the lens epithelium beyond the equator after long detachments. The total cataracts with pronounced changes

were found in the eyes with complete retinal gliosis. In the microphthalmic eye with the hyaloid artery and gliosis, proliferating capillary endothelium broke through the posterior part of the capsule.

*General Pathologic Features*—Congenital encephalo-ophthalmic dysplasia seems to affect the neuroectoderm primarily and the associated structures secondarily at an early fetal age. Development of the cerebral cortex may be retarded as early as the fetal age of 10 weeks. The basal ganglions and the brain stem are not evidently involved in the disease. Cerebral hyperplasia, hypoplasia and heterotopias are found. Hydrocephalus, if it occurs, is perhaps related to an anomalous development of the arachnoid membrane.

The development of the eye may be affected in early fetal life in the same manner. In the cases of severely affected development the manifestations are microphthalmos, malformation of the optic nerve head, and hyperplasia and hypoplasia of the retina. The intraretinal serous effusion and retinal detachment may follow later. The retina degenerates and atrophies. Posterior synechias form. Proliferation of the glia, mesodermal connective tissue and neuroepithelium may lead to the formation of a transverse retrolental membrane and of iridic and postlental capillaries. Intraocular exudation and hemorrhage, anterior synechias and cataracts are other complications. Secondary glaucoma is common. Leukocytic reaction is slight.

#### ETIOLOGIC FACTORS

The records of the 18 cases presented here served as the basis for a study of the origin of the disease. The recorded details permitted the grouping of factors that had a bearing on the causation.

*Hereditary and Familial Tendencies*—There was no evidence based on the statements of the parents that the disease was inherited directly from relatives in the mother's or the father's immediate family or in the ancestors. Furthermore, there was no second occurrence of the disease in the family in other, later pregnancies. Of course the value of family history was limited by the small number in the family, by the lack of knowledge concerning the relatives and by the great mobility of people under present social conditions. The only prominent hereditary factor not related to the disease was the presence of supernumerary toes in 1 child. This inheritance was traced to the father and the paternal ancestors.

The disease and prematurity were unrelated to the environment of the infant. The families were not in any one social stratum. The occupations of the fathers ranged from relief projects, employing the poverty-stricken, incompetent unemployed to the independent professions. Social conditions apparently were not related to the disease or to prematurity.

*Age of Father and Mother*—The range of ages of the fathers and mothers was similar to that of fathers and mothers of children without this ocular disease. There is no relation of the incidence of this disease to the age of the mother, like that which occurs with mongolism, or to later pregnancies, like that which is associated with the Rh factor. The distribution of the ages of the mothers at the time of birth was as follows: Three were from 15 to 20 years old, 4, from 21 to 25, 7, from 26 to 30, 1, between 31 and 35, 2, from 36 to 40 years, and 1, between 41 and 45. The distribution of the ages of the fathers at the time of birth was as follows: Three were from 20 to 25 years old, 6, from 26 to 30, 3, from 31 to 35, 2, from 36 to 40, 1 between 41 and 45, and 3 were of unknown ages.

*Time of Conception and Birth*—It was believed that the ocular and cerebral disease and prematurity might be related to an unknown infectious disease of the mother which might be more prevalent in certain months and seasons of the year. It was hoped that a study of the distribution of the times of birth and of the times of similar developmental stages of the fetus would give a clue to such a disease. When the month of conception was calculated from the gestational age, the distribution of the times of conception was remarkably evenly spaced throughout the year. The number of conceptions varied from 1 to 2 per month, and only once was it 3 per month. The distribution of births according to month of birth was regular, ranging from 1 to 2 per month except for one month, with 3 births. There was no predominance of births in a series of months or in any one season. But if the distribution of births is arranged according to months of the year, it appears that the 3 births in 1937 were between October 14 and December 22, in 1938, 4 were between February 4 and August 4, in 1939, 4 were between July 10 and November 20, and the others were scattered from 1941 to 1944. The calculation for the time of conception shows a definite nonseasonal grouping, which may be significant. The 3 infants born in 1937 were conceived between March and June, the 4 born in 1938 were conceived between July and November, the 4 born in 1939 were conceived in January and February, the 2 born in 1942, in July and October, the 2 born in 1943, in July, and the other 2, in 1943 and 1944. The records of the municipal and state health reports for this part of the country have given no suggestion of an increase in any disease which may be related to these periods.

*Number of Pregnancies*—Some diseases of infants and pregnancy are related to the number of pregnancies. Syphilis is a classic example of such a disease, the severity decreasing with the number of pregnancies. In the present cases, the infant was the result of the first pregnancy of 7 mothers, of the second pregnancy of 5 mothers, of the third pregnancy of 3 mothers, of the fourth pregnancy of 2 mothers.

and of the fifth pregnancy of 1 mother The distribution was in the range of the normal number of pregnancies Infants born of further pregnancies were not affected with the disease Each of the 18 infants was the only child in his family who had this ocular defect and the associated nervous disease

*Multiple Births*—Multiple births were found by Hess and associates<sup>8</sup> to be the most common single cause of premature labor In 4 of Terry's cases and in 1 of Wehrli's<sup>6</sup> series, the infants were twins In my 18 cases, there were 2 sets of twins and 1 set of triplets, all of whom were born between the twenty-ninth and the thirty-second week of pregnancy Only 1 infant survived in each set, the others died shortly after birth except for one of the triplets, who died at the age of 4 months Autopsy on 1 of these infants who died at birth showed nothing significant except for previability Although the number of multiple births in this series of cases was high in proportion to the single births, it was not suggestive of any definite positive connection with the disease except for prematurity There was no definite evidence for or against the presence of the disease in the other infant or infants of the multiple births except for the absence of any abnormality but previability in 1 child It was possible, but not probable, that the disease was not sufficiently developed to be observed clinically or to be detected in pathologic examination in the other child or children of the multiple birth The predominance of the neurodysplasia in infants from multiple pregnancies cannot be disregarded and may be a clue to the origin of the disease

*Sex of Child*—Sex apparently was not involved in the incidence of the disease It was slightly more frequent in females than in males Seven of the infants were males and 10 were females

*Race*—All infants were born of white parents, and no nationality was predominant In Providence Hospital for Negro patients no cases of the disease have been seen by the ophthalmologists

*Frequency*—The incidence of the disease was about 1 per 16,000 new patients attending the University of Chicago Clinics When the estimate was based on new patients from the time when the disease was first diagnosed to the time of writing, the ratio was 1 8,000 new patients The ratio of cases in Chicago Lying-In Hospital to the number of total births was 1 4,000 All the patients were born in Chicago or its suburbs except 1, who lived in a small city near Chicago

*Weight at Birth*—Some obstetricians place infants weighing less than 1,000 Gm at birth in the class of previable infants, which have an extremely high mortality rate, of about 99 per hundred The prema-

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<sup>8</sup> Hess, J H, Mohr, G J, and Bartelme, P F The Physical and Mental Growth of Prematurely Born Children, Chicago, University of Chicago Press, 1934



ture infants with a weight at birth of from 1,000 to 1,500 Gm have a death rate of about 25 per hundred. The premature infants weighing from 1,500 to 2,500 Gm have a good survival rate. If weight is used as the basis of judgment, then 13 infants were premature and 4 were mature. Four infants at birth weighed from 800 to 1,000 Gm, 4, from 1,000 to 1,500 Gm, 5, from 1,500 to 2,000 Gm, 2, from 2,500 to 3,000 Gm, 1, from 3,000 to 3,500 Gm, and 1, from 3,500 to 5,000 Gm. There was no doubt that the disease is commonly associated with small premature infants. The ratio in these cases is 13:4 in favor of prematurity. However, this disease is also associated with infants with a normal average weight at birth.

*Gestational Age*—The gestational age has always been difficult to estimate in weeks. It is usually based on the menstrual history. Only in unusual circumstances has it been determined exactly. For example, when soldiers have been home on a short leave of absence, the wives may know the date of conception. Generally the woman has a doubtful idea of the time interval. For this reason some obstetricians believe the gestational age may be missed by several weeks or by a month. Although most of the mothers were followed in the prenatal clinic, the weeks of pregnancy in these cases may vary in the same manner. When the weight of the child at birth does not accord with the gestational age, the menstrual history may be deceitfully or incorrectly given or may be naturally undeterminable.

Infants born with a gestational age of under 28 weeks are generally regarded as previable. Those who have a gestational age of less than 32 weeks have a mortality rate of about 25 per cent. Premature infants with a gestational age of between 32 and 38 weeks have a low death rate. It is believed by obstetricians that more premature infants, particularly in the early premature group, survive now and that many of the children with this disease fall in that group. However, some premature children have survived in the past, but the disease has not appeared to be associated with prematurity. In the report of Hess<sup>8</sup> on 200 cases of prematurity this disease was not seen in spite of careful observation and repeated examinations. In the 18 cases in the present series, the mothers gave a history of from 28 to 32 weeks of gestation in 12, of from 32 to 36 weeks in 2, of from 36 to 40 weeks in 1 and of 40 weeks in 3.

Although most of the patients were early premature infants, some were born at term. The ocular and cerebral disease occurred at birth or shortly after birth in the mature infants in the same manner and with the same severity as in the premature infants. The disease is frequently noticed later in premature infants than in mature infants because under the conditions of survival in an incubator the eyes are not observed or examined.

*Causes of Prematurity*—The precise etiologic factors influencing premature termination of pregnancy may be difficult to determine. Toxemia of pregnancy, in 3 mothers, multiple pregnancy, in 3, uterine bleeding, in 2, and premature rupture of the membranes, in 1, were the precipitating causes tending toward prematurity. On 1 of the mothers with toxemia of pregnancy a cesarean operation was performed.

The mothers were free of known syphilis and other infectious disease. In 1 woman the uterus was histologically normal. The placentas were not diseased in the 9 mothers from the Chicago Lying-In Hospital. The condition of the placentas of the other mothers was unknown. The cause of prematurity in the other 8 cases could not be determined in spite of careful examination of good hospital records and discussion of the cases with the obstetricians. A point of inquiry may be raised on the number of cases of prematurity without cause. The question of habitual miscarriage, numerous pregnancies at short intervals, under-nutrition of the fetus with premature expulsion and induced labor does not seem to arise here, although these points were investigated. It is possible that the disease causing cerebral and retinal dysplasia may tend also to cause prematurity, but there is no direct evidence except the frequency of this disease in premature infants. Seemingly, there is no specific disease of the uterus or of pregnancy associated with the dysplasia.

*Diseases of the Mother*—Since the prenatal and neonatal appearance of encephalo-ophthalmic dysplasia indicates that the mother may transfer the disease or the effects of disease to the fetus, a search was made for diseases of the mother. One mother had moderately severe essential hypertension, 3 had toxemia of pregnancy, 1 apparently had received treatments for syphilis, 1 had a cough and rapid loss of weight, and 12 had no disease. The Wassermann reactions of the mothers were negative. The blood counts were normal. There was no clinical evidence of lymphogranuloma venereum. The mothers of the patients who were born in 1943 and 1944 had no symptoms or signs of rubella or other exanthems during pregnancy. Unfortunately, questions to gain evidence on the presence of atypical virus pneumonia, ornithosis or psittacosis in the early months of pregnancy were not asked. All histories of colds, influenza, sore throat and cough in the patients were too vague to be of use as possible antecedents. It was believed that the clue to the cause of the disease was in the history of the mother in early pregnancy, but it was not found because of lack of a good method of attack. In spite of the negativity, it should not be permitted to be forgotten, as it may have a definite bearing on the origin of the disease.

*Neonatal Clinical Symptoms*—An attempt was made to correlate the neonatal clinical symptoms, such as cyanosis, jaundice and asphyxia,

with encephalo-ophthalmic dysplasia. Four infants had no unusual symptoms. One (case 10) of these 4 infants, a full term child, began to have convulsions after the age of 2 months and later died with a condition diagnosed post mortem as bronchopneumonia, cerebral agenesis and ocular dysgenesis. Another (case 14) of these infants, born of a full term pregnancy, was observed to have retinal masses in each eye within two weeks of birth. Later, according to the diagnosis from post-mortem examination, the child died of pneumonia and congenital hydrocephalus. The third child (case 11), an early premature infant, was born in another hospital, where the records showed no evidence of unusual symptoms, although the child was kept in an incubator. This infant was blind at birth and now is mentally retarded. The fourth child (case 2) of this group, an early premature infant, had retinal masses in each eye, which were first observed six months after birth. The child was normal at the age of 4 years except for blindness. There was no known factor in delivery of the child and no neonatal symptom or sign indicating the cause of the dysplasia in these 4 children.

One infant, born by cesarean section at a previsible age, had neonatal anemia with weakness and little vision.

Seven infants were cyanotic after birth. The ratio of 7:18 was about the same (53:102) as that attained by Hess.<sup>8</sup> Three of the 7 infants were cyanotic just after birth and recovered easily with oxygen treatment. The cyanosis of premature infants is generally related to atelectasis. The 4 infants with recurrent cyanosis probably had intracranial hemorrhage. Of these 4, 1 (case 1) died with hydrocephalus four years later. One (case 3) died of enteritis at 4 months of age. The brain histologically was normal. Another (case 4) was admitted to an institution for feeble-mindedness at the age of 6 years. The fourth had hemiparesis and cerebral agenesis. Two infants (cases 5 and 17), who were jaundiced several days after birth are living and well. Of 2 other infants with jaundice and recurrent cyanosis, 1 (case 9) with intracranial hemorrhage died at the age of 4 months with a condition diagnosed as congenital hydrocephalus and lissencephaly, and the other (case 7) was healthy and active mentally at the age of 7 years.

One child (case 15) had delayed respirations at birth. At the age of 4 months the child appeared to be normal mentally.

The histories in this small series unexpectedly showed no relationship of asphyxia, cyanosis and jaundice to hydrocephalus, severity of mental retardation and cerebral agenesis except in the infant with severe intracranial hemorrhage (case 9).

*Congenital Anomalies*.—The congenital anatomic anomalies were few, but they are not significant. Four infants possessed these mal-developments. There were bilateral talipes equinovarus, hemangioma of the occiput and chest, supernumerary toes and umbilical hernia.

*Other Possible Causes*—A further search for the origin of the disease was made. Rubella and similar exanthems of the mother in the first trimester of pregnancy were considered for some of the infants born in 1943 and 1944, after the reports by the Australians<sup>9</sup>. The cases at the University of Chicago Clinics in which the mother had rubella were excluded from this report. The symptoms and signs in these cases were the same as in previous reports. They were congenital cataract, low tone deafness, mental retardation, wide ductus arteriosus, defective interventricular septum and dental dysplasia. These signs are not those of neonatal encephalo-ophthalmic dysplasia.

The Rh factor was determined in 1 case, but there was no incompatibility between the blood of the mother and that of the child. There was no history or evidence of fetal erythroblastosis in the children of any multiple pregnancy.

Light as a factor has been considered by some ophthalmologists and pediatricians. Since 3 infants were born with the disease and 2 others probably had the disease from birth, there is little reason to suspect light as causing the damage to eyes in utero. Whether or not it is an additional factor after birth is still doubtful.

A toxic causation was investigated in a few late cases, but no history of poisoning with alcohol, lead, carbon monoxide, mercury, arsenic, apioi, quinine or tobacco was obtained.

One mother was examined and tested for brucellosis, but there was no indication that she had the disease.

Except for 1 case with probable treatment for syphilis and gonorrhea before pregnancy, there was no history of syphilis. All Wassermann reactions were negative.

Although there were no symptoms of toxoplasmosis in any mother and infant, the blood of 1 infant gave a negative reaction to the protective test. The pathologic sections of the brain and eyes after death showed no toxoplasmas.

In spite of the absence of any history of obvious symptoms of other virus diseases, it was unfortunate that there was no available method under the present conditions for testing the mother and child for the presence of the viruses causing atypical pneumonia, psittacosis and ornithosis. A virus infection was believed to be a possible cause of the disease.

*Chronologic Appearance*—The time of the first appearance of encephalo-ophthalmic dysplasia has an important bearing on the etiologic and pathologic features of the disease. If cases 9 and 10 are taken

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<sup>9</sup> Swann, C ; Tostevin, A. L., Moore, B., Mayo, H., and Black, G. A. Congenital Defects in Infants Following Infectious Disease During Pregnancy, *M. J. Australia* 30 201, 1943.

as illustrations of the earliest form of the disease, then the pathologic process begins in the first few months of pregnancy. In case 9 the postmortem diagnosis was bronchopneumonia, aplasia of the cerebral cortex and cerebellum, cerebral agyria, multiple heterotopias, congenital hydrocephalus, persistent hyaloid artery, congenital cataract, coloboma of the disk, retinal gliosis of the right eye and buphthalmos, congenital cataract and retinal gliosis of the left eye, and in case 10, bronchopneumonia, cerebral agenesis with multiple heterotopias and cyst of the cerebellum and bilateral retinal dysplasia. These changes occurred early in fetal life. In about the fifth week of fetal life the corpus callosum is formed. In both cases the agenesis of the corpus callosum was determined before the fifth week of embryonic life. After about the third month of embryonic development the cerebral gyri began to take their form. In case 9 the brain was agyric, in case 10 microgyria was present. In both cases the cerebellar aplasia probably was determined later than the agenesis of the cerebrum. The factor producing the subarachnoidal anomalies also was in effect after the second month of embryonic life. The hydrocephalus in case 9 was probably related to failure of development of the subarachnoid space. The heterotopias represented a further differentiation after a temporary arrest. Some tissues not differentiating further remained hypoplastic, and the revival in growth of tissue resulted in dysplasia or hyperplasia.

The ocular maldevelopment in case 9 occurred probably through arrested development of the initial retinal differentiation at the embryonic age of 3 months. The right eye was microphthalmic, and its retina showed dysplasia. The retina of the left eye was also maldeveloped and later was made atrophic in part by secondary glaucoma.

In case 8 the eyes and brain were affected by the sixth month of pregnancy.

*General Etiologic Factors*—Many probable general causes for the disease exist (Corner<sup>10</sup>). The problem may be summarized as follows:

- 1 Irregular fertilization may cause incomplete segmentation and death of the egg.

- 2 There is no evidence that this disease is related to a genetic defect.

- 3 It is possible, but not probable, that there is a relationship to a nongenetic constitutional defect. A comparable disease is mongolism. However, at present there is no good method of attack on this problem.

- 4 Delayed transportation of the egg through the oviduct frequently results in ectopic pregnancy and prominent defects. However, tubal pregnancy is not a factor in this disease.

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10 Corner, G. W. *Ourselves Unborn*, New Haven, Conn., Yale University Press, 1944, p. 108.

5 A failure of the hormone system causes early death of the embryo in animals. This effect has not been definitely observed in man.

6 A mechanical disorder of the uterus resulting in crowding of the embryo generally causes miscarriage at the end of the second or the third month.

7 Nutritional deficiencies, unless they are severe, have little effect on the embryo but a definite effect on the mother.

8 Infection of the genital tract tends to prevent fertilization and implantation of the egg.

9 Toxicity of the environment may cause maldevelopment. Roentgen radiation, radium, lead intoxication and the Rh factor are not apparent factors in the disease under discussion. Generally, a toxic reaction sufficient to affect the embryo affects the mother, and the cause of toxicity can be determined. Local intrauterine toxicity as a cause of developmental defect is difficult to prove.

10 The embryo may be infected with any of many organisms. Syphilis and smallpox are well known diseases of the fetus. Rubella, or German measles, recently was found to affect the embryo. If the mother had rubella during the first two months of pregnancy, the infant was frequently born defective. The abnormalities were congenital cataract, microphthalmos, deaf-mutism, patent ductus arteriosus, hypoplastic teeth, microcephaly and mental retardation. There is good reason to believe that the virulence of the virus of rubella may have changed and that the effect of this virus has not been recognized. The cases with a history of the mother's having rubella or symptoms of rubella were not included in this series. It is possible that another virus may be the cause of encephalo-ophthalmic dysplasia.

## SYMPTOMATOLOGY

### OCULAR SYMPTOMS

The study of ocular symptoms in the 18 cases gave information on diagnostic errors, on the differential diagnosis and on the chronologic features and clinical variation of the disease.

*Time of Onset*—The probable time of onset of the disease was difficult to determine in some infants because the early symptoms were not observed, the abnormalities were not investigated and the eyes were not examined, or, if they were, the examination was inadequate. In cases 8, 9, 10, 11, 14 and 17 the eyes were affected before birth. According to the histologic observations on the eyes in cases 9 and 10, the disease was evident in the early fetal stage, and in case 8 the retina had been detached and then reattached before birth. In case 17 the retinal maldevelopment which was disclosed by clinical observation was similar to that of falciform fold and stalks of the retina, which is an early embry-

onic defect In the other cases, 11 and 14, vision was poor at birth, and the retinal mass was seen just after birth In 4 cases the retinal defect was probably present before the first few weeks of life, in 3 cases, before 2 months of age, in 2 cases, before 3 months of age, in 1 case, long before 6 months of age, and in 2 cases, long before 9 months of age If the symptoms are discovered late, the disease is usually mild, and the early stages are overlooked Terry noted that the retinal disease in his cases was always visible before 6 months of age<sup>1f</sup>

*Time of First Observation*—The time of first observation of the ocular defect varied remarkably for a serious disease which occurs at birth or in the early weeks of life In 3 cases the defect was noticed at or near birth, in 2, in the first month, in 3, from the first to the second month, in 3, from the second to the third month, in 1, from the third to the fourth month, in 4, from the fourth to the sixth month and in 2, from the sixth to ninth month In almost every case the disease was far progressed The time interval between the initiation of the disease and the time of detection is related to the lack of training in ophthalmoscopy in medical schools and the lack of habitual use of the ophthalmoscope in medical examinations

The ocular symptoms were usually missed by the physician either because no examination was made or because it is difficult to examine the eyes of recently born infants This also explains why retinoblastoma is often not observed until the mother notices an ocular defect The mother was the first observer of an ocular defect in 5 cases, the pediatrician, in 7 cases, commonly because of careful routine examination, the obstetrician, in 3 cases, and the family physician, in 3 cases

*First Prominent Symptoms*—The most prominent symptoms noticed by the first observer, mother or physician, were blindness, in 14 eyes, retinal mass, in 10 eyes (by the physician), large size of the bulb, in 3 eyes, small size, in 1 eye, white pupils, in 2 eyes, and yellow pupils, in 2 eyes In 4 eyes no abnormality was noticed The blindness was often discovered at home when the mother cared for the child It was apparently not detected by the nurses when the infant was in the Hess bed

*First Tentative Ophthalmic Diagnosis*—In few cases was the first tentative diagnosis the same as the final diagnosis One reason was that only an examination with the child under general anesthesia was satisfactory At first the tendency was to consider the retinal mass a retinoblastoma Later, after more experience, a different conception of the retinal mass was obtained In 21 eyes the diagnosis was retinoblastoma, in 6, retrolental fibroplasia, in 4, myopia, in 3, pseudoglioma, and in 1 each, atrophy of the optic nerve, microphthalmos, retinal detachment and secondary glaucoma In 1 eye the disease was missed

*Bilaterality*—In every case the disease was bilateral. In 12 cases bilateral retinal detachment occurred. In 3 cases unilateral retinal detachment with atrophy or dysgenesis of the retina and optic nerve was evident. One case of bilateral retinal gliosis was seen, and 1 case each of bilateral retinal hypoplasia and bilateral congenital retinal folds was found.

The retinal detachment in one eye and the dysplasia of the retina in the other eye gave evidence that the bilateral retinal dysplasia probably belonged to the same group of defects. The early retinal gliosis was perhaps based on different embryonic timing of the same disease process. The congenital retinal folds were part of a similar process. These eyes showed the various possible forms the disease may take. However, in no case was one eye free of disease.

*Position of Hands*—The position of the back of the hands over the eyes to avoid light, which was mentioned by Terry,<sup>1</sup> was characteristic in those infants who were unaccustomed to bright light and in whom the retinal detachment was in the early stages. It was not unusual for the infant to act in the same manner when it was photophobic to light on the iris during mild irritative nitis or when it was suffering pain from the secondary glaucoma or the induced glaucoma which arises from crying.

*Vision*—Vision ultimately was decreased or totally lost in all cases. In the eyes with congenital myopia and retinal dysplasia but without detachment vision was generally never above perception of shadows and movements and of light in space. The child often misled the examiner by detection of objects by smell and not by sight. In 1 case the child recognized the odor of the father's leather coat and would turn toward the source of the odor. Response to the local heat of a light gave misinterpretations of vision. Infants with fixed congenital retinal folds and stalk or infants just before detachment of the retina or with partly detached retinas noted the direction of the light. A few had vision for larger forms. In all cases of detachment vision was reduced in time to light perception or became nil.

*Ptosis*—Ptosis was noticeable in 5 infants. In 4 it was unilateral and in 1 bilateral. Of the infants with unilateral ptosis, the defect was on the left in 3 and on the right in 1. In all cases the ptosis was related to the disease, for it occurred only with microphthalmic eyes, with the eye of smaller size and with more severe disease. It could not be definitely associated with the intrauterine position of the infant or with method of delivery. Endophthalmos seemed to be apparent in 1 of the infants with ptosis. Each eye was microphthalmic, and the smaller eye appeared to be endophthalmic.



*Strabismus*—The external ocular movements were unrestricted in all cases. In infants totally blind at birth the movements remained irregular and were not conjugated. If light perception persisted until just after birth in one eye only, the conjugation was poor. If light perception persisted a few weeks after birth, the movements were roving and inconstant but conjugated. In 4 infants the eyes showed occasional convergence, and in 1 the left eye turned in 20 degrees. In 1 infant slight paresis of the left external rectus muscle disappeared when he became older.

*Microphthalmos*—The size of the bulb was difficult to determine in a restless infant. It was estimated by measuring the diameter of the cornea, by comparison of the size of one eye with that of the other and with the size of normal eyes of infants of the same age, and by comparison of the enucleated eyes with normal eyes. The transverse diameter of the cornea was estimated in 27 eyes. Microphthalmos was evident bilaterally in 8 cases and unilaterally in 4 cases. In 5 cases the size of the eyes was not abnormal. In the 5 cases of myopia the retinas were at the upper limit of normal size or were larger than normal eyes of infants of the same age. Early, long-continued detachment occurred with small corneas and small eyes. Early and pronounced glaucoma, usually of long duration, gave rise to a large globe. One globe was large at birth (case 9).

*Synechias*—The anterior chamber was shallow in 22 eyes and collapsed in 8 eyes. The decrease in depth of the chamber occurred with the retinal detachment and once with retinal dysplasia associated with myopia.

Iridic synechias are common to the eyes with this disease, particularly those with detached retinas. Anterior synechias were observed clinically in 4 eyes and were not noted in many eyes with shallow, collapsed anterior chambers. Five eyes were observed pathologically to have anterior synechias which were not noticed clinically. In 1 eye a particular effort was made to find anterior synechias clinically, but they were seen only after section.

*Pupillary Reactions*—The pupillary reaction to light before retinal detachment was apparently active in almost all eyes. After the detachment started, the pupils became sluggish in reaction and later became fixed. The fixation was the result of posterior synechias. In 5 eyes with little or no pupillary reaction to light no posterior synechias were observed clinically, and the irises were probably sticky. In these eyes the pupils dilated with atropine. The pupils in the eyes with retinal gliosis, dysgenesis and myopia became fixed early. In the 18 infants, 24 pupils became fixed, 6 showed some signs of reaction, and the remainder were not closely observed.

*Glaucoma*—The abnormally high intraocular pressure was determined with difficulty. In 9 eyes of 5 patients there were signs of glaucoma. The tension, which, when taken, was estimated either by the Schiøtz or by the Souter method while the child was under ether anesthesia, was often subject to misinterpretation. A thin cornea, small eye, collapsed anterior chamber, straining child and lack of a standard for infants were factors which prevented the use of instrumental methods. The bulbar conjunctiva became reddened in 3 eyes with severe glaucoma. Other such eyes often were redder than usual after crying, but this reaction may be related also to mild irritative iritis present with the detached retina. However, reddened eyes were not common with glaucoma. A fugitive corneal haziness in 3 eyes was caused by glaucoma. This sign was probably overlooked in many other eyes, or the infant was not seen at the proper time.

At some stage of the disease increased intraocular tension was obtained in the clinic in 9 eyes, either by tactile or by instrumental measurement. These eyes showed injection of the conjunctiva and a steamy cornea with the rise in intraocular pressure. In some eyes the glaucoma was observed only when the infant cried. The glaucoma generally followed the posterior synechias or intraocular hemorrhages. It lasted for weeks or months, and then the eye tended to become softer. In case 9 the left eye had a congenital hydrophthalmos but not buphthalmos. The congenital incomplete development of the filtration angle was an added factor in glaucoma. Some microphthalmic eyes were of average size because of the glaucomatous pressure.

*Fetal Vascular System*—Persistent pupillary membranes and vessels were more commonly present in the eyes of the early premature infants shortly after birth and in the eyes with marked malformations or retinal detachments in full term infants. Vessels of the iris extended over or onto the pupillary opening in 4 eyes after, but not before, the retinal detachment. They were not seen in several eyes.

The hyaloid artery was not evident in the premature eyes. If vascular remnants of the hyaloid artery were present, they could not easily be found in the detached retinas on gross examination. The hyaloid artery was not observed in the microphthalmic eye, in which it was later seen in section, because of the obscuration from an anterior hyaloid membrane.

A vitreous membrane was believed to be present in 4 eyes. The membrane was not positively identified in sections in 1 eye and was related retinal folds in another. In 1 eye (case 9, right eye) it was dense and was seen to extend from the ora serrata in the sections.

The white and black dentate processes of the ciliary body were observed in 4 eyes. Two of these eyes had retinal folds. Unfortunately, search for dentations was made only in a few late cases. This

observation, first noted by Lane<sup>2t</sup> and later by Terry, was an aid in diagnosis of non-neoplastic disease

*Lens*—The lens was clear in nearly all eyes. In the infant with gliosis, the lens of one eye was slightly hazy, and the other was believed to have a yellow nodule near or in the posterior cortex. Another lens showed a few translucent cortical striae. In an eye with retinal folds extending to the posterior capsule, the lens was cataractous at the place of contact, but the other lens seemed clear. In 1 infant with retinal detachment both lenses became hard cataracts. The other lenses, when displaced toward the cornea and when in eyes with glaucoma of long duration, became cloudy, but the haze of the cornea prevented close observation.

*Retina*—The most common feature was the retinal disease. The varieties of disease have been given in the discussion of its occurrence in the eyes. In the eyes with dysplastic, undetached retina, the disk was pale as though atrophic. In some eyes it appeared slightly colobomatous. In highly myopic eyes and in 1 nonmyopic eye the retinal vessels seemed smaller than normal. In 1 eye they were crowded to the side of the disk. The fundus reflex was not so brilliant and red as normal. The macular reflex was absent. In 2 eyes white circular areas, rimmed lightly with melanotic pigment, were scattered around the disk. They tended to increase slowly in size. Retinas with congenital folds have been described by Ida Mann<sup>11</sup> in numerous articles.

The retinal detachment was seen as a solid, roughened, grayish red mass of retina. The roughened retina was quite characteristic in the early process of detachment. The detached mass came forward like a funnel. Occasionally one side was more prominent than the other. The retina then appeared detached on one side, and on the other the reflex of the choroid gave a picture of a blurred reddish retina. If the detached retina became thin, the red choroidal reflex was seen. The retinal vessels disappeared in the center of the roughened retina in cases of total detachment. In a few eyes hemorrhages occurred in the retina and appeared as a dark red, brown-black mass just behind the lens. If a larger hemorrhage occurred, the whole retina was suddenly crowded against the lens, which, in turn, was pushed toward the cornea. If the retina was partly detached, examination by means of the slit lamp or fine beam and proper magnification, with the patient under general anesthesia, showed the dentate processes of the ciliary processes. The long processes were white and fused with the light-colored detached retina. The spaces between the dentation were black in the early stages of the disease, after the retina atrophied the spaces showed the red choroidal reflex.

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<sup>11</sup> Mann, I. *Developmental Abnormalities of the Eye*, London, Cambridge University Press, 1937.

## GENERAL NEUROLOGIC SYMPTOMS

There were no special pathognomonic symptoms of the neurologic disease. The two common symptoms were hydrocephalus and, especially, mental retardation. The mental retardation was related to lack of cerebral development and to the effects of hydrocephalus, which in 1 case at least was associated with the anomaly of the arachnoid membrane. The basal ganglions, brain stem and spinal cord were not involved in the dysplasia, if they were affected, their disease probably had a different origin.

*Hydrocephalus, Microcephalus and Cerebral Agencsis*—Hydrocephalus occurred in 4 cases. Blockage of the intercommunicating system was the main cause. One infant (case 8) was known by roentgenographic examination to have extreme hydrocephalus in utero and of necessity was delivered by cesarean section. The child died one day after birth. At autopsy the whole brain collapsed to an unrecognizable mass.

In case 9 extreme congenital hydrocephalus and a large intracranial hemorrhage were present at birth. In this case the blockage was related to congenital maldevelopment of the arachnoid structure. Presumably, in the other cases the hydrocephalus was due to a similar maldevelopment.

In case 14 signs of hydrocephalus were first noticed at the age of 1 month. Trepanation showed a thin cortex and dilated ventricles secondary to obstruction of the ventricular system. This was confirmed at autopsy at the age of 1 year and 8 months.

In case 6 the hydrocephalus began to be obvious six weeks after birth. It became extreme and caused the death of the infant at the age of 5 months. At autopsy fibrous adhesions were observed to block the aqueduct.

In the 2 infants with heads of normal size at birth the ventricles may have been dilated before birth, for the intrauterine pressure tends to prevent expansion of the skull and the head may enlarge in the following months. One infant showed bulging fontanel and separation of sutures only when the dehydration was overcome. The yellow fluid in the ventricles in case 14 was probably due to rupture of small veins by the traction arising from the hydrocephalus.

With hydrocephalus occurred the usual symptoms, such as convulsions, vomiting, cyanosis, lethargy and spasticity. Many of the other common congenital defects associated with congenital hydrocephalus, i. e., meningocele, porencephaly, spina bifida and cranium bifidum, were not present. In 2 of the 4 infants with hydrocephalus there was no retinal detachment but dysplasia of the retina and atrophy of the optic nerve. In 2 infants the retinas were detached. As the roof of the orbit was depressed, the bulbs were pushed downward and outward.

Cerebral agenesis was diagnosed in 3 cases (12, 13 and 16), and microcephalus with hydrocephalus, in 1 case (10). The same pathologic processes which led to hydrocephalus in other cases apparently produced cerebral agenesis and the secondary microcephalus in these cases.

*Other Neurologic Symptoms Not Pertaining to the Disease*—Other neurologic symptoms not particularly related to the disease were cephalohematoma, subdural and subarachnoid hemorrhage (case 9), hemiparesis (case 13), spastic quadriplegia (case 16) and cerebral spastic palsy (case 18).

*Mental Retardation*—Mental retardation was noted in almost every infant. Ten infants were definitely retarded, and 3 were probably retarded. In 2 infants the mentality could not be determined. Two infants were normal. Psychometric tests on 5 children indicated low mentality. It was impossible to give suitable tests to many of the children because of loss of eyesight, the effect of the protective environment at home, the age of the infant and lack of suitable standard methods of testing, which are yet to be developed.

The tests for mental retardation were difficult to apply to these children. The circumstances of their life were different from normal infants of their age. Lack of vision, protective environment and prematurity are relatively unknown factors in testing. There is little experience or information on which to base a judgment as to the mentality of these infants. A careful history and repeated intelligent observation of the child's behavior gave a better idea of the mentality than testing.

The Kuhlmann intelligence rating which covers the period from 3 months to 2 years of age was determined for a few of the most adaptable children by an experienced child psychologist. In case 1, the Kuhlmann intelligence quotient was 41, in case 11, 39, and in case 10, 5, in cases 12 and 18 the mentality was low grade but could not be estimated numerically.

The Gesell tests were quite useless here for intelligence rating, for they depend mainly on motor reactions. It was surprising that the blind infant in case 1 had a Kuhlmann intelligence quotient of 41 at the age of 3 years, was considered mentally normal two months later by expert state psychologists and psychiatrists and then died within two months of a "brain tumor."

*Final Disposition*—Encephalo-ophthalmic dysplasia was more than static blindness and mental retardation after the age of 6 months. In some infants it was progressive, and in others it was arrested or partly arrested. It would not be surprising if hydrocephalus should develop later in childhood in infants who do not show it. All these children should be followed for a lifetime.

Seven infants with the dysplasia have died. Autopsies showed that 1 died at birth of hydrocephalus, 1, at 13 weeks of age of acute enteritis; 1, at 4 months of pneumonia, 1, at 5½ months of hydrocephalus, 1, at 1 year 5 months of bronchopneumonia, 1, at 1 year 9 months of pneumonia, and 1, at 3 years 5 months of a "brain tumor." Three infants were placed in institutions for the feeble-minded. Their ages in January 1945 were 1, 3½ and 7 years. Three infants, aged 1½, 2½ and 5½ years, are feeble physically and retarded mentally. Three infants, aged 5½, 7 and 5½ years, are healthy. The condition of 2 infants, aged 2½ and 3½ years, is unknown at present.

### DIFFERENTIAL DIAGNOSIS

The retinal disease most likely to be confused with this disease is retinoblastoma and pseudoglioma. The other diseases which may simulate encephalo-ophthalmic dysplasia are relatively easy to diagnose.

*Retinoblastoma*—If there is reasonable doubt whether or not a retinoblastoma is present, a decision must be made on the removal of the eye. However, there are certain common characteristics of encephalo-ophthalmic dysplasia which help to differentiate between the two diseases. They are (1) prematurity, (2) congenital defective vision, (3) bilaterality or ocular disease, (4) congenital retinal anomalies, (5) microphthalmos, (6) central radiating blood vessels on the rough surface of a central retinal mass, (7) prominent dentate processes of the ciliary body, (8) recurrent retrolental hemorrhage and (9) early mental retardation.

The contrasting signs and symptoms of retinoblastoma are (1) roentgenographic evidence of ocular calcification, (2) disseminated foci of tumor in some eyes, (3) occurrence usually later in life, (4) occasional evidence of familial tendency, (5) generally unilateral occurrence, and (6) masses with typical smooth, glistening surface.

*Metastatic Enophthalmitis*—A history of meningitis, otitis media, scarlet fever, measles, mumps or other infectious disease is related to the retinal detachment or mass behind the lens. In cases without a history of infection, the pain and redness of the eye, the photophobia, fever, rash, convulsions, spasticity, vomiting and coma are suggestive of metastatic enophthalmitis.

*Tuberculosis*—A tuberculoma is generally unilateral. The infant will show other signs of tuberculosis, and the tuberculin test gives a positive reaction. Exposure of the child to tuberculosis will be evident from the presence of the disease in some one who is in close contact with the child.

*Syphilis*—Congenital syphilis of the eye is associated with other physical signs in the mother and child. The Wassermann reactions of the mother and of the child are often positive.

*Rubella*—Detachment of the retina has occurred with rubella. It may be impossible to obtain a history of rubella in the mother in early pregnancy. Lenticular opacities are usually visible before any retinal changes are seen. The infant may have a large ductus arteriosus, deafness to low tones, mental retardation and dental aplasia.

*Retinal Ghosis*—Ghosis of the retina resulting from hemorrhages is extremely rare in infants. The lesion tends to be localized as a clearcut, permanent retinal plaque. Ghosis of the entire retina with other signs was found in 1 case of encephalo-ophthalmic dysplasia.

*Retinal Folds*—The retinal folds which were described by Mann<sup>11</sup> are commonly familial. They are a result of a congenital maldevelopment of the vitreous and retina which is not progressive and which may occur in one or both eyes.

*Persistent Hyaloid Artery*—Some of the points of difference in eyes with persistent hyaloid vascular systems are unilaterality, absence of detached retina, nonprogressiveness of the process and absence of mental symptoms and history of prematurity.

### TREATMENT

The medical and surgical treatment of retinal dysplasia is unsatisfactory. The instillation of solutions of pilocarpine is perhaps not the proper method to reduce the congenital secondary glaucoma in the presence of posterior synechias. The application of solutions of atropine to overcome the formation of posterior synechias and secondary glaucoma tends to cause greater blockage of the immaturely developed filtration angle. The use of radium or roentgen radiation to reduce vascularization and proliferation of glial and mesodermal connective tissue has had questionable success and may actually stimulate tissue proliferation.

In most cases with retinal detachment an operation, such as trepanation for the reduction of the intraocular pressure, may not give relief from the glaucoma. There is always the question whether or not retinal and retrolental hemorrhages will be more frequent and severe when the pressure is reduced. Since the iris and the ciliary processes are involved in the disease, the operation may be useless and may result in more damage to the eye. In the cases with secondary glaucoma without retinal detachment a trepanation may be a valuable method of treatment.

In the case of an eye which has vision and which has a congenital cataract with congenital retinal folds, retrolental and ciliary membranes or anomalous vascularization which is fixed and not undergoing changes, an operative procedure on the membranes or vessels of the lens, to give sufficient opening through the pupil, may be considered. The technical details for each operation must be planned before surgical attack. Cata-

tract extraction in eyes with total retinal detachment is useless. Of course, surgical correction of the massive retinal detachment is as yet impossible.

If the eye is red and painful from uncontrollable secondary glaucoma or if there is reasonable doubt concerning glioma, an enucleation of the eye arises as a problem for decision. In some eyes the high intraocular pressure decreases as the retina atrophies ;

### SOCIAL SIGNIFICANCE

*Medical*—If children with this defect are affected in utero by a specific disease of the mother during early pregnancy, it is important to determine the disease which produces the maldevelopment. The question would then arise whether the pregnant woman affected with the disease should have her pregnancy terminated to prevent the chance of birth of a defective child. Whatever the cause of the dysplasia, the disease is sufficiently frequent and severe to merit attention to prevention. A blind, mentally retarded child is a social burden.

*Social*—It is important to determine the mental status of the infant early by competent and experienced child psychologists. If the child is feeble-minded, he should be committed to an institution as soon as it can be done. If the infant or child is at home or in a similar environment, the special protective reaction of the mother, relatives or attendants may greatly hinder the development of the mind and may also create behavior problems. It is difficult to judge mental retardation in such circumstances. A congenitally blind healthy child will respond to proper social treatment in a remarkable manner.

*Legal*—There is good probability that some of these infants may be adopted by foster parents. The laws concerned with adoption are considered to give the most irrevocable contract known legally. If an infant with this disease is legally adopted, the adoption later cannot be annulled. The adoption of a child is an act of faith and hope in any case, in spite of the best preadoption examination and investigation of the child and his relatives. A happy future for the perfect child is expected, but not guaranteed. Except in cases of severe disease, it is unlikely that the cerebral symptoms in a young infant will be noticed in examination by the average physician. If the retinal lesion is not obvious, or if it develops after the first few months of life, the ocular defect may not be observed until after adoption. The examination of an infant under 1 year of age is restricted by the lack of detailed knowledge and standards, so that it cannot compare with a similar examination performed later in life. Mental tests on infants are notoriously unsuccessful. Mental retardation, unless it is extreme, is difficult to detect, as evidenced by this series of cases.



A legal case of this kind has been presented in court. The infant was considered to be healthy by a physician before adoption. Shortly after adoption the infant had difficulty in seeing. On examination the child was found to have the retinal dysplasia. The foster parents of the child are now suing for annulment of the adoption.

#### SUMMARY

Eighteen cases of congenital encephalo-ophthalmic dysplasia of unknown origin are described. The neuroectodermal disease was more commonly found in premature infants and in single infants of a multiple birth. The common neurologic signs were mental retardation, microcephalus and hydrocephalus. In some cases the brain, on histologic examination, showed cerebral and cerebellar hyperplasia, hypoplasia and agenesis, heterotopias and internal hydrocephalus. Clinically, the ocular disease rarely occurred without neurologic signs of involvement of the brain when the child was examined after the age of 4 years.

The ocular signs were loss of vision, ptosis, enophthalmos, microphthalmos, strabismus, retinal detachment, postlental masses, retinal atrophy, gliosis, recurrent retinal and vitreous hemorrhages, anterior and posterior synechias, secondary glaucoma and cataract. The hyperplasia, hypoplasia and dysplasia of the retina and colobomas of the choroid and optic nerve were accompanied with malformations of the associated mesodermal tissue.

No method of treatment was found to prevent or to cure the disease.

The common disposition of a child with the severe form of the disease was commitment to a state institution for the feeble-minded or to an institution for the blind. Death from intercurrent infection frequently occurred.

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# ETIOLOGY AND TREATMENT OF BLEPHARITIS

A Study in Military Personnel

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**B**LEPHARITIS is a chronic inflammation of the lid border. It can be divided into two general types: (1) the squamous type, characterized by hyperemia of the lid border with dry or greasy scales, and (2) the ulcerative type, characterized by the development of small pustules involving the follicles of the cilia and leading to the formation of small ulcers. Conjunctivitis and superficial keratitis commonly accompany both types.

Blepharitis is the most common external ocular inflammation seen in military personnel and is an important cause of disability, both in itself and as the source of a number of disabling complications. It is of distinct military importance because the symptoms characteristic of the moderately severe and acute forms, which include burning and smarting, epiphora, photophobia and asthenopia, interfere definitely with the efficiency of the soldier. These symptoms appear to be particularly troublesome in air crew members and to be exaggerated during high altitude flying. The complications range from internal and external hordeolums, meibomitis and chalazion to chronic conjunctivitis, marginal ulceration of the cornea and, rarely but importantly, trichiasis and entropion. Although it is not generally recognized, even very mild forms may be the source of chronic catarrhal conjunctivitis. Of relatively minor importance, but not to be ignored, is the cosmetic aspect of the disease. The unsightly scaling, redness and epiphora may constitute a definite morale factor in military personnel.

In many clinics the significance of blepharitis is apparently underestimated, and soldiers complaining of the disease are neglected in the sense that they are often given prescriptions without follow-up care of any kind. Since the most important clinical feature of blepharitis is its chronicity, unsupervised home treatment is almost inevitably unsatisfactory. Determination of the etiologic factor, moreover, is in most cases a prerequisite for adequate therapeutic management, which in any event requires frequent observation and a judicious rotation of procedures in all but the mildest type.

The frequency and severity of blepharitis seem to be definitely increased under tropical conditions. Its military importance was,

therefore, relatively greater in the recent war as a result of the concentration of troops in the South Pacific area

Textbook discussions of blepharitis have long seemed to me to be regrettably inadequate with respect to both etiology and therapy. In spite of general recognition that the disease is not an etiologic entity, there has been a tendency to consider it a clinical entity to be treated without regard to causative factors.

A survey of the literature reveals that a wide variety of etiologic possibilities have been advanced. The more significant of these are as follows: (1) bacteria, including staphylococci, streptococci and diplobacilli, (2) allergy to various substances, (3) fungi, (4) errors of refraction, (5) seborrhea, (6) animal parasites, (7) vitamin deficiencies, (8) endocrine disturbances, and (9) hereditary predisposition. In his excellent review on blephoritis published in 1929 Aubaret<sup>1</sup> discussed these factors in detail and reviewed the literature adequately to that date. Since then the few etiologic studies reported have been devoted largely to a consideration of the role of pathogenic staphylococci in the disease. The reports of Burky,<sup>2</sup> Allen<sup>3</sup> and Thygeson<sup>4</sup> indicated that toxin-producing staphylococci were probably the most important single etiologic feature and that antistaphylococcic therapy was an improvement over older therapeutic measures.

In undertaking this study, it was proposed to define all possible etiologic factors and to evaluate therapeutic procedures in a series of unselected cases of blepharitis observed in Army personnel. The series presented no unusual aspects other than that the patients were, with few exceptions, young adults. There is every reason, therefore, to believe that the disease as seen in this series is representative of blepharitis in the civilian population. The condition in these cases ranged in severity from the mild, almost subclinical type to the severe, ulcerative type with conjunctival and corneal complications. Of these, 350 were available for complete etiologic analysis, but in a number of cases Army transfers interfered with the completion of therapeutic studies.

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1 Aubaret, E. *Etiologie et traitement des blepharites*, Paris, Masson & Cie, 1929, *Bull et mem Soc franç d'opht* **42** 1, 1929, *Arch d'opht* **46** 372 (June) 1929.

• 2 Burky, E. L. *Studies on Action of Staphylococcus Toxin and Anti-Toxin with Special Reference to Ophthalmology*, *Am J Ophth* **19** 841 (Oct) 1936.

3 Allen, J. H. *Experimental Production of Conjunctivitis with Staphylococci*, *Am J Ophth* **22** 1218 (Nov) 1939, *Staphylococcic Conjunctivitis Experimental Reproduction with Staphylococcus Toxin*, *ibid* **20** 1025 (Oct) 1937.

4 Thygeson, P. (a) *Bacterial Factors in Chronic Catarrhal Conjunctivitis Role of Toxin-Forming Staphylococci*, *Arch Ophth* **18** 373 (Sept) 1937, (b) *Treatment of Staphylococcic Conjunctivitis with Staphylococcus Toxoid Preliminary Note*, *ibid* **20** 271 (Aug) 1938, (c) *Staphylococcic Blepharitis*, *Tr Am Acad Ophth* (1941) **46** 265 (July-Aug) 1942.

Not included in the series were cases of marginal blepharitis seen in connection with such dermatologic conditions as exfoliative dermatitis, pityriasis rosea and herpes simplex. As a minor manifestation of a generalized disorder, the involvement of the lid margin in these cases differed from typical marginal blepharitis in being self limited. Two cases of pityriasis rosea, for example, which were referred by Capt Morris Waisman, M C, A U S, chief of the dermatologic section of the hospital, showed a squamous type of blepharitis which was obviously part of the widespread, symmetric, patchlike eruption characteristic of the disease. In both cases healing was spontaneous in about six weeks. Two cases of herpes simplex of the eyelids with involvement of the lid margins were also seen, but in both the lesions cleared rapidly without residual blepharitis.

## I ETIOLOGY

Comprehensive clinical and laboratory studies were made routinely in the search for features which might have etiologic significance. The clinical survey included examination of the following associated parts. (1) the scalp, for evidence of dandruff, (2) the face, for infections of the skin, such as seborrheic dermatitis and acne rosacea, and for evidence of seborrhea, (3) the external ears, for otitis externa, (4) the tongue, lips and corneal limbus, for clinical signs of vitamin B complex deficiency, (5) the conjunctiva and cornea, for Bitot's spots and keratinization as evidence of vitamin A deficiency, (6) the cornea, with fluorescein, for evidence of catarrhal infiltration or ulceration and punctate epithelial staining of the type characteristic of staphylococcic infection, (7) the meibomian glands, with expression, to determine the existence of hyperactivity or meibomitis, and, finally, (8) the lid margins, to determine, by means of gross and biomicroscopic observation, the clinical type of the blepharitis (whether ciliary or meibomian, ulcerative or nonulcerative), the type of scales (whether dry, tenacious or greasy) and the condition of the cilia (whether infected or otherwise abnormal).

In addition to this objective examination, the patient was questioned on the following points: (1) duration of the disease, (2) history or presence of known staphylococcic infections, such as sties or boils, (3) dietary habits, with particular reference to vitamin deficiency and to the abnormal use of fats and sweets, and (4) history or presence of pruritus or of other allergic manifestation, such as hay fever, urticaria or eczema, with particular inquiry into the possibility of sensitivity to drugs. All patients who had abnormal vision or complained of symptoms of asthenopia were given refraction.

Laboratory studies included examination of routine scrapings from the lid margins with cultures of the material and cultures of secretions

of the conjunctiva when conjunctivitis was a prominent feature. Conjunctival smears were taken when there was conjunctival secretion or when the history suggested the possibility of allergy. When there was complicating meibomitis, expressed meibomian material was studied for cell content and bacteria. When the patient complained of excessive itching, the slides were examined for conjunctival eosinophilia. Other laboratory procedures included the use of special mediums for fungi and the testing of pathogenic staphylococci for sensitivity to penicillin and sulfonamide drugs. Patch tests were used as an aid in the diagnosis of contact dermatitis.

#### LABORATORY DATA

Table 1 summarizes the laboratory findings in scrapings from the lid margins and cultures in 350 cases of blepharitis. The scrapings from the lid margin yielded only four significant forms: (1) budding yeast forms, (2) cocci, (3) diplobacilli and (4) polymorphonuclear leukocytes. Diphtheroids, considered of no etiologic importance, were

TABLE 1—*Micro-Organisms in Scrapings from Lid Margins in 350 Cases of Blepharitis*

|  | Number of Cases |
|--|-----------------|
| Budding yeast forms, only                      | 100             |
| Pathogenic staphylococci, only *               | 130             |
| Hemophilus duplex                              | 4               |
| Mixed yeast forms and pathogenic staphylococci | 102             |
| Alpha streptococci                             | 3               |
| Beta streptococci                              | 2               |
| Coliform bacilli                               | 1               |
| Proteus bacilli                                | 2               |
| Normal flora                                   | 6               |

\* Coagulase positive *Staphylococcus aureus* and *Staphylococcus albus*

also usually present. The bacterial cultures yielded only two significant organisms: (1) staphylococci and (2) diplobacilli. Beta hemolytic streptococci were isolated (simultaneously with *Staphylococcus aureus*) in 3 cases, alpha hemolytic streptococci in 2 cases, a coliform bacillus in 1 case and a proteus organism in 2 cases. Diphtheroid bacilli and isolated colonies of nonpathogenic white staphylococci were also commonly found.

*Budding Yeast Forms*—In the scrapings from the lid margin the budding yeast forms, occurring often in large numbers, were by far the most conspicuous finding. They were morphologically identical with similar forms found in dandruff (seborrheic dermatitis) and known as *Pityrosporum ovale*. Round forms predominated over oval, flask-shaped forms. Cultivation of the organism on beer wort agar was obtained with some difficulty by Capt. Joseph Gots, Sn C, A U S, and, together with other observations on *P. ovale*, will be the subject of a later communication.

The role of *P. ovale* in seborrheic dermatitis is still unsettled, but it is believed by some observers<sup>5</sup> to be the primary cause of the disease, with the acne bacillus and *Staphylococcus albus* acting as secondary factors. Whether or not this will prove to be true, it seems to have been definitely established that large numbers of the organism are invariably found in cases of the disease. To test the usefulness of its demonstration as a diagnostic sign of seborrheic blepharitis, scrapings

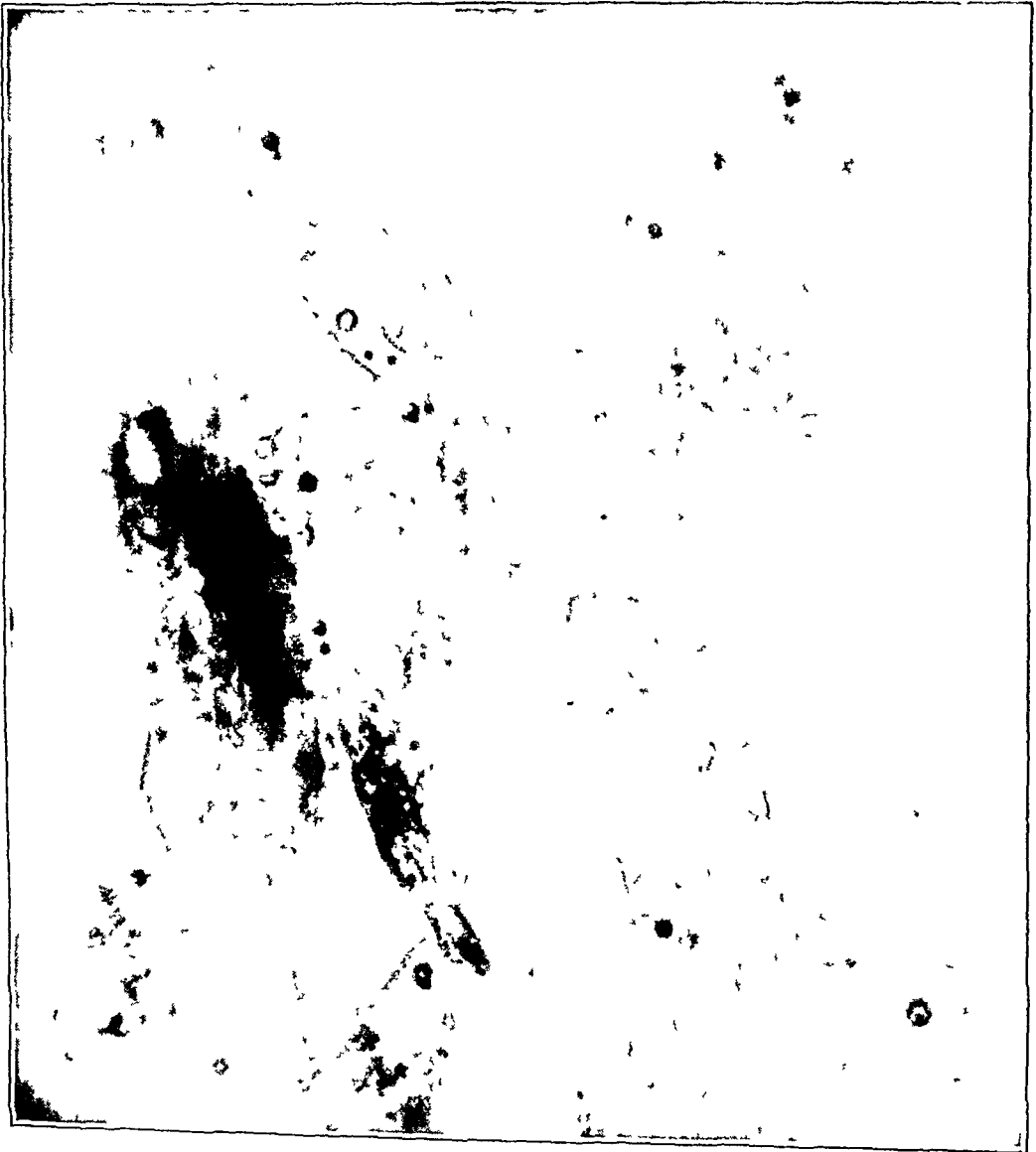


Fig 1—*Pityrosporum ovale* in scrapings from the lid margin in a case of blepharitis,  $\times 900$

<sup>5</sup> Moore, M., Kile, R. L., Engman, M. F., Jr., and Engman, M. F. *Pityrosporum Ovale* (Bottle Bacillus of Unna, Spore of Malassez) Cultivation and Possible Role in Seborrheic Dermatitis, *Arch Dermat & Syph* **33** 457 (March) 1936. Kile, R. L., and Engman, M. F. Further Studies of the Relation of *Pityrosporum Ovale* to Seborrheic Eczema, *ibid* **37** 616 (April) 1938.

from a series of 25 lid margins which appeared normal on examination with the slit lamp and which had not previously been inflamed were examined for the organism. In 2 specimens only were isolated yeast cells observed. On the other hand, every one of a series of scrapings from 25 blepharitic lid margins, which were negative for pathogenic staphylococci and diplobacilli but with which there was associated seborrheic dermatitis of the scalp, face or external ears, contained large numbers of the organism. It would seem legitimate, therefore, to attach at least some diagnostic value to this finding.

*Cocci*—The demonstration in scrapings alone of gram-positive cocci would appear to have little diagnostic significance, since it is not possible by morphologic differences alone to distinguish pathogenic from nonpathogenic staphylococci. Culture study in numerous cases, however, indicated that pathogenic staphylococci are the only cocci occurring in sufficient numbers in cases of blepharitis to be of significance in the examination of scrapings from the lid margins. I therefore now consider the demonstration in scrapings of both gram-positive cocci and polymorphonuclear leukocytes to be a fairly reliable diagnostic sign of staphylococcic blepharitis. It should be emphasized, however, that this finding is present only in severe cases.

Certain diagnosis of staphylococcic infection can be made most reliably by means of blood agar cultures. An attempt has been made in this study to differentiate sharply between pathogenic and nonpathogenic staphylococci on the basis of the coagulase test and mannitol fermentation. These presumptive tests for pathogenicity are now widely used and have been shown to be reasonably trustworthy, with the coagulase test the more valuable of the two. In general, it can be stated that most strains of *Staph aureus* are pathogenic and most strains of *Staph albus* are nonpathogenic. In table 1 it will be seen that presumably pathogenic staphylococci were recovered from 130 of the 350 cases of blepharitis. Pathogenic staphylococci thus constitute the most important single finding in this series of cases.

It should be noticed that the concomitance of P. ovale and pathogenic staphylococci was observed in 102 cases.

*Diplobacilli*—*Haemophilus duplex* (Morax-Axenfeld diplobacillus) was demonstrated in only 4 cases, but in these it occurred in large numbers and was also demonstrable in smears of the conjunctival secretion. Since this organism is known to be highly parasitic, its demonstration on the lid margin can certainly be considered an indication of its etiologic significance. No polymorphonuclear leukocytes were found in association with the diplobacilli, a finding consistent with the known fact that diplobacilli are not pyogenic.

*Other Organisms*—The significance of beta hemolytic and alpha hemolytic streptococci in blepharitis is difficult to evaluate, but as

they are known to attack the scalp and other areas of the skin, it is probable that they are occasionally concerned in blepharitis. The role of beta hemolytic streptococci in impetigo is well known. In the present series alpha streptococci were recovered in 3 cases and beta streptococci in 2.

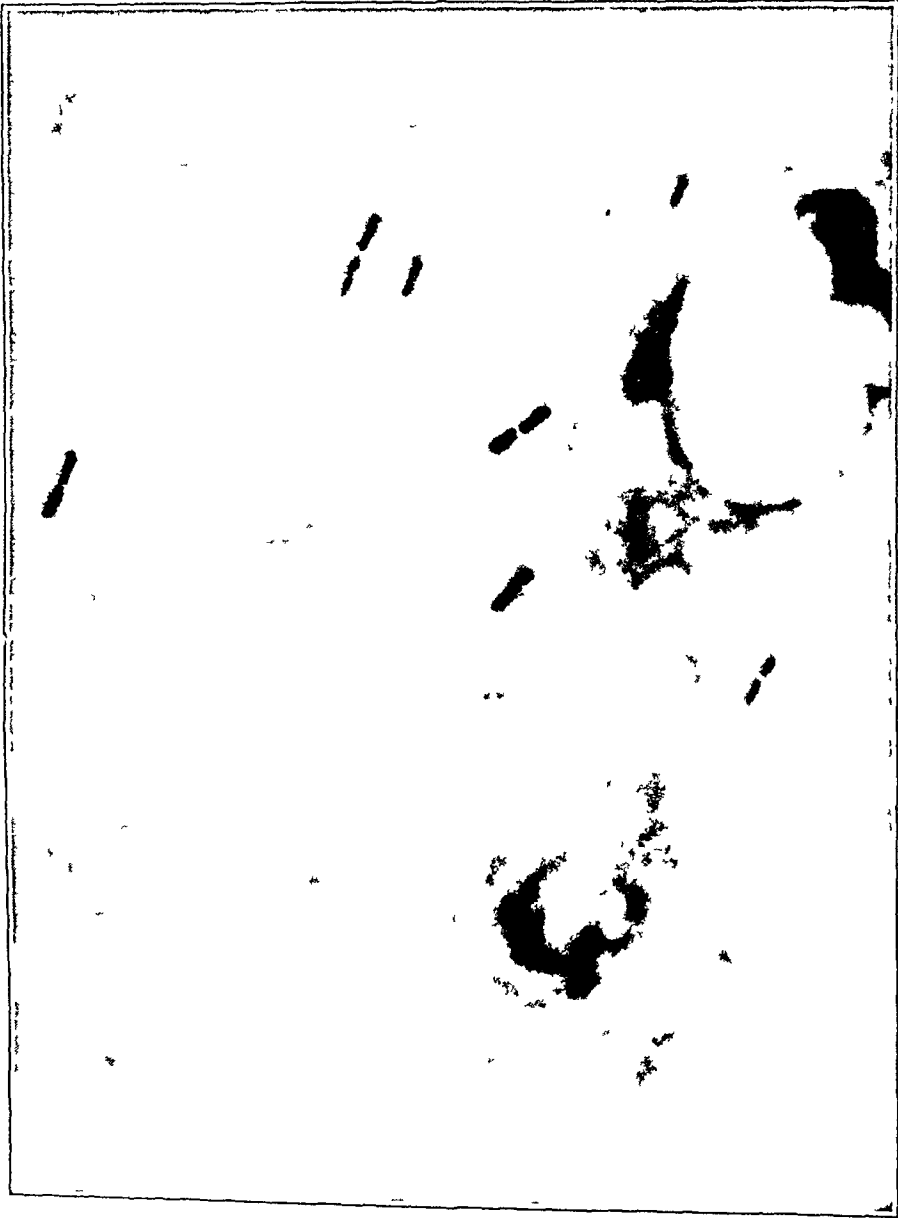


Fig 2—*Haemophilus duplex* (Morax-Axenfeld diplobacillus) in scrapings from the lid margin in a case of blepharitis due to this organism,  $\times 900$

Coliform bacilli were found in a single case and proteus bacilli in 2 cases. These organisms are occasionally found as probable causal agents in conjunctivitis, but there is no evidence to indicate that they can attack areas of the skin and therefore no reason to attach etiologic significance to these isolated findings.



In view of the frequency of ringworm infections in this geographic area, a special search was made for ringworm fungi in scrapings and cultures from the lid margins. It is noteworthy that not a single case of this infection was found.

#### ETIOLOGIC TYPES OF BLEPHARITIS

A comparative study of laboratory and clinical findings revealed that only three important etiologic types of marginal blepharitis could be distinguished in this series. These were (1) blepharitis due to seborrheic dermatitis, (2) blepharitis due to pathogenic staphylococci and (3) blepharitis due to *H. duplex* (Morax-Axenfeld diplobacillus). Their characteristics are summarized in table 2. There was a high incidence of mixed seborrheic and staphylococcic blepharitis.

TABLE 2—*Characteristics of the Three Principal Types of Blepharitis*

|  | Staphylococcic<br>Blepharitis   | Seborrheic<br>Blepharitis  | Blepharitis Due to<br><i>Hemophilus Duplex</i> |
|--|---|--|--|
| Seborrhea capitis  | Occasionally present  | Always present   | Occasionally present                           |
| Associated dermatoses                                      | Acne vulgaris,<br>rosacea, impetigo,<br>infectious eczematoid<br>dermatitis, sycosis<br>barbae, boils | Seborrheic derma-<br>titis of brows<br>and external<br>ears frequent | Occasionally dermatitis<br>at external nares   |
| Bilateral or unilateral                                    | Unilateral involve-<br>ment not uncommon  | Always bilateral   | Unilateral involvement<br>not uncommon         |
| Ulcerative or nonulcera-<br>tive                           | Frequently ulcerative   | Never ulcerative   | Never ulcerative                               |
| Associated hordeolum                                       | Frequent  | Rare or absent   | Rare or absent                                 |
| Associated conjunctivitis                                  | Frequent and often<br>severe  | Minimal or absent  | Always present                                 |
| Associated keratitis                                       | Punctate epithelial<br>erosions generally<br>present, marginal<br>infiltrates and<br>ulcers common    | Absent   | Marginal infiltrates<br>and ulcers common      |
| Scales and crusting  | Hard, tenacious<br>scales, removable<br>with difficulty   | Greasy scales,<br>easily removed                                     | Macerated epithelium<br>with minimal scaling   |
| Microscopic examination<br>of scrapings from lid<br>margin | Staphylococci and<br>leukocytes   | Budding yeast<br>forms ( <i>Pityro-<br/>sporum ovale</i> )           | <i>H. duplex</i> , no<br>leukocytes            |

*Seborrheic Blepharitis*—The following clinical characteristics were present in the blepharitis believed to be due entirely to seborrheic dermatitis. 1 There was always an associated seborrhea capitis, usually of from moderate to severe intensity, with a history of annoying dandruff. 2 An associated seborrheic dermatitis of the brows and external ears was present in a significant number of cases. 3 The blepharitis was always nonulcerative and squamous in character, and the scales were greasy and easy to scrape off. 4 Associated conjunctivitis, if any, was minimal, and in only a few cases was there any punctate staining of the cornea, a feature highly characteristic of staphylococcic infection. 5 The symptoms were always minimal, the patient in many cases being unaware of the presence of the disease. 6 There was

no characteristic association with hordeolum or furunculosis 7 The disease was characteristically bilateral, no single case of unilateral involvement being demonstrated in this series 8 The skin of the face usually, though not always, showed evidence of increased sebaceous activity.

In connection with this clinical picture, which could be considered diagnostic without laboratory study in most instances, scrapings from the lid margin always showed budding yeast forms identical with the *P. ovale* believed to be characteristic of seborrhea capitis

It should be emphasized at this point that pure seborrheic blepharitis was less common than mixed seborrheic and staphylococcic blepharitis There was a strong suggestion, in fact, that the principal role of the seborrheic infection was to prepare the soil for secondary staphylococcic involvement, with its relatively severe symptoms and complications While seborrheic blepharitis is not in itself disabling, its importance as a cosmetic blemish is considerable, the red lid margins and greasy scales being conspicuously unattractive

*Staphylococcic Blepharitis*—The following important clinical characteristics of blepharitis in which pathogenic staphylococci were the only significant findings were noted in this study 1 Unilateral disease was frequently seen, particularly in cases of recent onset The disease was often limited to a single portion of the lid margin, moreover, or involved one lid almost to the exclusion of the other It is noteworthy that symptoms were always more severe when the upper lid was involved predominantly, perhaps because gravity permitted scales and infectious material to fall into the conjunctival sac more frequently 2 The blepharitis was often ulcerative and was commonly associated with recurrent hordeolums and chalazions 3 The scales were small, hard, tenacious and sometimes extremely difficult to remove 4 Associated keratoconjunctivitis was almost the rule This was sometimes extremely severe and appeared to outweigh in importance the blepharitis which was believed to be its primary focus In cases of mild keratitis only punctate epithelial staining appeared, principally of the lower halves of the cornea, but in cases of the more severe form there were marginal infiltrates and ulcers, which were always associated with formation of new vessels 5 Temporary or permanent loss of cilia was a feature of the ulcerative type 6 Other dermatologic associations were common, particularly otitis externa, impetigo, sycosis barbae and infectious eczematoid dermatitis Acne vulgaris was frequently present 7 Symptoms of burning, itching, photophobia and eyestrain were associated with all but the very mildest forms

The characteristic pathologic pictures of all types of staphylococcic dermatitis were observed in the infections of the lid margins of this series, as follows 1 A typical eruption of superficial pustular folli-

culitis, characterized by yellow pustules pierced by hairs, was seen in a number of cases. This infection was limited to the upper third of the hair follicles. 2 The lesions of furunculosis were reproduced in the form of hordeolum, usually single, but sometimes conglomerate and affecting the entire lid margin. The pathologic nature of this lesion is abscess involving the deep part of the hair follicle and its sebaceous gland. 3 Sycosis vulgaris, also called barber's itch, was represented. It resembled superficial pustular folliculitis except for its great severity, perifolliculitis with abscess formation developing. 4 The characteristic lesions of impetigo, which may be of either streptococcic or staphylococcic origin or of both were seen on numerous lid margins. The primary lesion is a red macule, which rapidly becomes a flaccid vesicle and eventually a pustule. After rupture the seropurulent exudate dries, leaving thick, honey-colored crusts. Removal of the crusts discloses superficial ulcers. 5 Infectious eczematoid dermatitis was often seen in relation to blepharitis, and the typical eczematoid eruption, characterized by edema, crusting and weeping, was observed on the lid margin proper. The lesions varied from a very mild type, papular or scaly with little infiltration, to an acutely inflamed type with local edema, pustulation and heavy crusting.

On the basis of these observations, one would clearly be justified in describing staphylococcic blepharitis in terms of its dermatologic equivalents, e. g., impetiginous blepharitis, infectious eczematoid blepharitis, furuncular blepharitis and superficial pustular follicular blepharitis. There would seem to be no particular advantage, however, in complicating the present, generally used, classification of ulcerative and nonulcerative staphylococcic blepharitis, which is roughly adequate for clinical purposes.

*Blepharitis Due to Hemophilus Duplex*—1 The principal clinical characteristic of this infection was its angular localization, with maceration of the skin at the inner and outer canthi. 2 An associated conjunctivitis was invariable and always prominent. 3 The infection was always superficial, showing no tendency to involve the meibomian glands, and there were no associated hordeolums. 4 The condition was never ulcerative. 5 Punctate staining was rare and, when present, differed strikingly from the punctate staining of staphylococcic infection in showing larger and fewer punctate points. Marginal corneal infiltrates and ulcers did not occur in any of the few cases of this series, but I have seen them in a number of civilian cases.

It should be emphasized that the blepharoconjunctivitis due to *H. duplex*, while rare in this series, occurs commonly in other parts of the country. I<sup>6</sup> found it to be very prevalent among the Apache

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6 Thygeson, P., and Forster, W. G. Observation on Trachoma of the White Mountain Apache Indians, Proc. Sixth Pacific Sc. Cong. 5: 879, 1939.

Indians of Arizona and to have occurred in almost epidemic form in a mental institution near New York city. No explanation can be given for its low incidence among soldiers at the air field where this study was made in view of the fact that they were drawn from all parts of the United States and were thus unusually representative of the country as a whole.

*Mixed Seborrheic and Staphylococcic Blepharitis*—Mixed seborrheic and staphylococcic blepharitis was the second most common type found in the present series. The diagnosis was made on the simultaneous demonstration of pathogenic staphylococci and large numbers of P. ovale in the lesions. Clinically this form resembled the pure seborrheic form more closely than the pure staphylococcic form except that there were usually conjunctival and corneal complications.

The 4 cases of H. duplex blepharitis studied were apparently pure in that no pathogenic staphylococci were found in cultures and no P. ovale in scrapings from the lid margins. In civilian cases, however, I<sup>7</sup> have often seen H. duplex blepharoconjunctivitis mixed with staphylococcic blepharitis, and no doubt it occurs with seborrheic blepharitis.

#### BLEPHARITIS IN ASSOCIATION WITH OTHER DISEASE

*Acne Rosacea*—Blepharitis complicating acne rosacea is a common finding in civilian practice, but, surprisingly, only 1 case was seen at this air field in the course of the present study. In this case the blepharitis was moderately severe and complicated with meibomitis. That the ocular manifestations were due in large part at least to infection with pathogenic staphylococci was indicated by the striking relief obtained from antistaphylococcic therapy. The importance of pathogenic staphylococci in blepharitis associated with rosacea has been stressed by Wise,<sup>8</sup> who found that none of the lesions of rosacea were influenced by riboflavin.

*Pediculosis*—Pediculosis as a cause of blepharitis was considered in 2 cases of phthiriasis palpebrarum discovered at this air field, but in 1 case the presence of pubic lice and nits on the lashes did not lead to symptoms of blepharitis, and in the other blepharitis was present but cultures revealed pathogenic staphylococci. That the blepharitis was due to staphylococci rather than to the pediculosis was indicated by the fact that it persisted after the pediculi were eliminated. These observations were in accordance with my previous experience with phthiriasis palpebrarum in civilian life, in which the parasites produced minimal changes in the lid margin.

<sup>7</sup> Thygeson, P., and Braley, A. E. Local Therapy of Catarrhal Conjunctivitis with Sulfonamide Compounds, Arch. Ophth. **29** 760 (May) 1943.

<sup>8</sup> Wise, G. Ocular Rosacea, Am. J. Ophth. **26** 591 (June) 1943.

*Trachoma*—Four cases of blepharitis were observed in patients with trachoma. In all 4 cases pathogenic staphylococci were recovered from the lid margins and were presumed to be causal. Blepharitis is not a manifestation of trachoma, as the virus does not attack the lid margins. It must, therefore, be considered a complication caused by superimposed infection with staphylococci or *H. duplex*.

#### INVOLVEMENT OF THE LIDS WITHOUT MARGINAL BLEPHARITIS

Numerous cases of allergic dermatitis of the eyelid were noted, but as the dermatitis involved the entire area of the lids and tended to spare the margins they were eliminated from consideration as cases of typical marginal blepharitis. No single case of true allergic involvement of the lid margins was observed. This is in sharp contradiction to Lemoine,<sup>9</sup> who stated that allergy is a frequent cause of blepharitis.

A case of lichen planus with predominant involvement of the lids was seen, but the margins were spared.

As has already been noted, it seemed logical, in view of the high incidence of ringworm infection in troops stationed in Florida, to expect instances of infection of the lid margin with fungi of the ringworm group. A few such cases have been reported in the literature,<sup>10</sup> notably in children. At this air field no single case of marginal involvement was recognized, although 2 cases were seen with ringworm of the lid proper. These presented no diagnostic problem whatever.

#### IMPORTANCE OF MILD OR SUBCLINICAL BLEPHARITIS

Early in this study it became evident that blepharitis was a far more common disease than had generally been supposed. Routine examination of the lid margin with the slit lamp and corneal microscope in all cases of chronic conjunctivitis revealed a high incidence of inflammation of the lid margins which would have been missed if gross examination alone had been relied on. Biomicroscopically, however, differentiation between normal and pathologic lid margins could be made easily. Differentiation could also usually be made in this way between pure seborrheic and pure staphylococcic blepharitis, since the greasy scales of the seborrheic type look quite different microscopically from the dry, fibrinous flakes of the staphylococcic type. Many of these cases of biomicroscopic or subclinical blepharitis could be recognized

<sup>9</sup> Lemoine, A. N. Allergies in Ophthalmology, Arch Ophth **28** 79 (July) 1942.

<sup>10</sup> Mata Lopez, P. Arch Soc oftal hispano-am **2** 62 (Jan-Feb) 1943.  
Costa, O. G. Microsporon Infection of Palpebral and Ciliary Regions, Arch Dermat & Syph **48** 65 (July) 1943.  
Sivers, S. H. Microsporon Audouinii Infection of the Eyelashes, ibid **49** 436 (June) 1944.

by examination with the ordinary loupe once attention had been called to them from study with the slit lamp

In view of the well known causal relationship of blepharitis to conjunctivitis, it is clear that careful examination with the slit lamp of the lid margins in cases of chronic conjunctivitis should be made routinely. The conjunctiva could be treated indefinitely without result if the primary focus were in the lid margins and ignored. In my opinion, the importance of biomicroscopic examination in these cases cannot be stressed too highly.

#### SECONDARY ETIOLOGIC FACTORS IN BLEPHARITIS

*Role of the Meibomian Glands*—In the majority of cases of blepharitis in this series involvement was limited entirely to the ciliary region of the lid margin, with complete sparing of the meibomian area. In these cases the meibomian glands showed no evidence of hypersecretion or of infection. Other cases were seen, however, in which, in addition to involvement of the ciliary area, the meibomian area showed hyperemia and maceration of the epithelium with dilatation of the meibomian orifices and hypersecretion and infection of the glands. It was in these cases that frequently recurring attacks of internal hordeolums and chalazions occurred. Smears from infected glands showed numerous leukocytes, with occasional scattered cocci and diphtheroid bacilli but no yeast forms or diplobacilli. The meibomitis was frequently spotty in character, perhaps only one or two glands on the entire lid margin being affected. It was noted that infection was rare in the absence of hypersecretion and that when it did occur it was in the form of internal hordeolums rather than of chronic meibomitis. In cases of chronic meibomitis atonic glands were found which had become converted into "pus pockets." A number of cases were seen in which isolated infected meibomian glands appeared to constitute foci for the continuance of the staphylococcic blepharitis.

*Role of Vitamin Deficiency*—Recent studies<sup>11</sup> on vitamin B complex deficiency indicate that it may be a factor both in seborrheic dermatitis and in susceptibility to staphylococcic infection, and a deficiency of vitamin A has been suggested<sup>12</sup> as an etiologic factor in acne vulgaris, a disease shown to be related in some of its manifestations to blepharitis. For these reasons, the cases of blepharitis in this series were studied for clinical signs of vitamin deficiency, particularly Bitot's spots and prexerotic signs, extension of limbal capillaries,

11 Gross, P. Non-Pellagrous Eruptions of the Skin Due to Deficiency of Vitamin B Complex, *Arch Dermat & Syph* **43**:504 (March) 1941.

12 Saunders, T. S. Favorable Effects of Vitamin A in a Case of Acne of Long Duration, *Arch Dermat & Syph* **50** 199 (Sept) 1944. Straumfjord, J. V. Vitamin A. Its Effect on Acne, *Northwest Med* **42** 219 (Aug) 1943.

cheilosis and strawberry tongue. No clinical manifestations of vitamin A deficiency were noted, however, or any signs which could be attributed with any certainty to vitamin B complex deficiency. There was only 1 case of perleche in the series. In this case the lesion was unilateral, contained pathogenic staphylococci and yielded to antiseptic therapy alone. In the only other case of perlèche observed no blepharitis or other ocular signs were present. In a considerable number of cases there was extension of limbal capillaries into the cornea, but the significance of this sign as evidence of riboflavin deficiency has been thrown into doubt by many observers<sup>13</sup>

The patients were questioned as to their dietary habits, but in no case was there evidence of a grossly inadequate diet, past or present. This is in accordance with the findings of the officers of the medical service in this hospital, who have discovered no clinical cases of vitamin deficiency at this field and consider the Army diet maintained here to be adequate in vitamin A and vitamin B complex. As will be described later, the use of vitamin preparations did not noticeably affect the clinical course of blepharitis in 25 cases in which it was tried.

A number of patients reported excessive intake of fats or sweets or both, and some of these men were grossly overweight. Since excessive intake of fats could be a factor in the hypersecretion of the meibomian and sebaceous glands of the lid margin, and since excessive intake of sugar is known to increase susceptibility to staphylococcic infection, both excesses were curtailed in these patients. Such dietary improvement, however, resulted in no observable change in the blepharitis.

*Role of Refractive Error*—Most textbooks mention the importance of correction of refractive errors in the treatment of blepharitis. Although it is somewhat difficult to see any direct connection between the two conditions, it is conceivable that eyestrain could result in congestion of the lid margins, with consequent hypersecretion of the meibomian glands and increased susceptibility to infection. As has also been claimed, refractive errors might possibly produce irritation of the lids, which would result in rubbing the lids with soiled fingers and thus lead to their infection. From the findings in 190 refractions, summarized in table 3, it seems unlikely, however, that refractive errors played any considerable part in the production of blepharitis in this series. It is of interest that the 2 patients with the most severe infection had 20/20 vision in each eye and showed only insignificant hyperopic errors on cycloplegic refraction. The patients receiving glasses for correction

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13 Scarborough, H. Circumcorneal Injection as a Sign of Riboflavin Deficiency in Man, *Brit M J* **2** 601 (Nov 21) 1942. Scott, J. G. Corneal Vascularity as Sign of Ariboflavinosis, *J Roy Army M Corps* **82** 133 (March) 1944. Sebrell, W. H. Nutrition in Preventive Medicine, *J A M A* **123** 342 (Oct 9) 1943.

of refractive errors were carefully questioned as to whether or not they felt that the wearing of the glasses alleviated their symptoms. While a few claimed that their eyes felt more comfortable with the glasses, the general opinion was that the disease had not been noticeably influenced.

*Role of Personal Hygiene*—There was some evidence in this series to indicate that Army conditions, particularly in the heat and glare of Florida, caused exacerbations of blepharitis. There were a number of soldiers who stated that although the condition had been present since

TABLE 3—*Refractive Errors in 190 Cases of Blepharitis*<sup>1</sup>

|                                | Number of Cases |
|--------------------------------|-----------------|
| Emmetropia                     | 41              |
| Myopia                         | 22              |
| Low                            | 3               |
| Moderate                       | 12              |
| High                           | 7               |
| Hyperopia                      | 15              |
| Low                            | 15              |
| Moderate                       | 0               |
| High                           | 0               |
| Hyperopic astigmatism          | 12              |
| Low                            | 11              |
| Moderate                       | 0               |
| High                           | 1               |
| Myopic astigmatism             | 5               |
| Low                            | 5               |
| Moderate                       | 0               |
| High                           | 0               |
| Mixed astigmatism              | 13              |
| Low                            | 12              |
| Moderate                       | 1               |
| High                           | 0               |
| Compound hyperopic astigmatism | 42              |
| Low                            | 26              |
| Moderate                       | 12              |
| High                           | 4               |
| Compound myopic astigmatism    | 26              |
| Low                            | 15              |
| Moderate                       | 16              |
| High                           | 5               |

\* Low error means less than 1.00 D, moderate error, 1.00 to 3.00 D, high error, 3.00+ D

childhood they had never had serious trouble with it until entering military life. The main factor seemed to be the difficulty of maintaining personal cleanliness under field conditions, which tended to increase staphylococcal infections of the skin generally.

*Role of Allergy*—As previously noted, allergy appeared to play no etiologic role whatever in marginal blepharitis in this series, although there were a number of cases of allergic involvement of the entire lid area due to drug sensitivity and contact dermatitis caused by cosmetics. There were no cases in which the onset of the blepharitis could be ascribed to an allergic sensitivity, but it is certainly conceivable that a contact dermatitis might lead to secondary staphylococcal infection, which, in turn, might induce a staphylococcal blepharitis. No examples



of such a sequence were observed, however. Numerous cases of allergic conjunctivitis due to pollens were studied, but no single case of blepharitis was found among them. In 3 cases of vernal catarrh with secondary staphylococcic infection moderately severe staphylococcic blepharitis and meibomitis were present, but most vernal catarrh, as seen in civilian practice, is not accompanied with blepharitis, and it seems unlikely that the association of the two conditions in these 3 cases was other than accidental.

*Role of Heredity*—There appears to be a definite hereditary factor in blepharitis. In a significant number of cases in this series there was a history of familial occurrence, particularly in parents and grandparents. This hereditary predisposition was stressed by Aubaret and was noted by me in previous studies on staphylococcic blepharitis. It is, of course, possible that communicability of the disease accounts for the familial occurrence, but its failure to spread from husband to wife, or vice versa, as was noted in this series, is indicative of a low degree of communicability. Just what the hereditary factors concerned consist in could not be ascertained in this study. The well known susceptibility of blond skins to blepharitis was observed, however, the disease being relatively rare among brunette and Negro troops.

*Role of the Endocrine Glands*—The role of endocrine factors could not be determined in this series. The relationship of seborrhea to the endocrine glands is well recognized, however, and leaves small doubt that they play a part in many cases by contributing to the hyperactivity of the sebaceous and meibomian glands, which, in turn, increases the susceptibility of the lid margins to the development of blepharitis.

#### COMMENT

In view of the steady advances currently being made in specific therapy of infectious disease, it is increasingly important to determine the etiologic factors in ocular disease. The cause of many ocular infections is still unknown and many are not specific entities. It is evident from this and other studies that blepharitis is by no means an etiologic entity but has a varied etiology, comparable to that of other infections of mucocutaneous junctions, such as *perlèche*<sup>14</sup>. It is also suggested by this study that mixed infections are almost as common in blepharitis as pure infections.

In the absence of direct lid inoculation experiments with staphylococci, the pathogenic role of these organisms in blepharitis must be assumed on the basis of present knowledge of the staphylococcic dermatoses. It is well known that staphylococci have a special predilection

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14 Finnerud, C. W. *Perlèche: Its Nosologic Status*, J. A. M. A. **126** 737 (Nov. 18) 1944.

for the skin and attack this tissue in various ways to produce the clinical pictures, for example, of impetigo, infectious eczematoid dermatitis and folliculitis. These types of cutaneous reaction were seen in the cases of staphylococcic blepharitis of this series. Furthermore, the etiologic relation of staphylococci to certain types of blepharitis is clearly evident from therapeutic studies in which elimination of the organisms resulted in rapid healing of the disease and failure to do so resulted in its persistence.

It is difficult to make a clear distinction between pathogenic and nonpathogenic staphylococci in spite of the numerous studies which have been made on the subject. The criterion used in this series, i. e., the ability of the organism to give a positive reaction to the coagulase test, is certainly not 100 per cent reliable. On clinical grounds it is suspected that certain coagulase-negative strains of *Staph. aureus* are pathogenic for the lid margins, but further studies will be required to prove or disprove this suspicion.

In the interests of speculating on the origin of the infection of the lid margin, an attempt was made to obtain the history of onset in each case. While the data secured were not sufficiently reliable to warrant statistical analysis, certain information of value was obtained. Most patients with staphylococcic blepharitis gave a history of onset in childhood. Certain of these men recalled definite onset after measles, impetigo, acute conjunctivitis or hordeolum. In the few cases of recent onset the blepharitis usually followed an attack of sties or of acute conjunctivitis. It is well known that pathogenic staphylococci are found very commonly in the nose, particularly in the external nares. It is safe to assume that transfer of organisms from this reservoir to the eyelids by way of fingers or handkerchiefs frequently occurs.

The etiologic role of seborrheic dermatitis in blepharitis must be assessed on clinical grounds alone, since the cause of the cutaneous disease itself is still in dispute. The etiologic relation of the two conditions is clinically apparent, however, from the identity of the lesions of the lid margin with those of seborrheic dermatitis of the scalp and brow. It is probable that *P. ovale* will eventually be shown to be the etiologic agent. It was constantly present in the cases of seborrheic blepharitis of this series, and its demonstration in large numbers in scrapings from the lid margins is advanced as a diagnostic sign in spite of the fact that small numbers are occasionally found on the clinically normal lid. In this series the correlation between laboratory and clinical findings in cases of seborrheic blepharitis was found to be very close.

Blepharitis due to *H. duplex*, which has long been recognized as a disease entity, was surprisingly infrequent in this series considering the fact that it is known to occur commonly in various parts of the country. Diagnosis is not difficult, as the organisms are usually numer-

ous in scrapings from the lid margins and identifiable on morphologic grounds alone, so that cultural studies are unnecessary. In the 4 cases in this series the typical involvement of the angles was present, but in a few cases of pure staphylococcic origin this clinical feature was also displayed, so that diagnosis on strictly clinical grounds is not completely reliable. It is known that *H. duplex* is also frequently found in the nose, particularly in the external nares. It is likely, therefore, as has been presumed for staphylococcic blepharitis, that many cases of blepharitis due to this organism arise as a result of transfer of infectious material from the nose.

It is of interest that with but few exceptions a cause could be assigned to every case of blepharitis. This, of course, does not mean that determination of the etiologic agent was accurate in every case, but it does indicate the probability that the common causes of blepharitis are limited to a relatively few agents. In isolated cases, of course, a variety of agents not found in this series may well be the cause. It is believed, however, that this study clearly shows that the ordinary ringworm fungi are not commonly concerned in the disease, since ringworm was prevalent among the patients of this series and the tropical conditions of Florida were conducive to spread of the infection. In spite of this, not a single instance of infection of the lid margin was noted among these patients. It seems probable from this study that streptococci, particularly beta-hemolytic streptococci, can occasionally produce or contribute to the production of blepharitis but that they do so rarely.

*Demodex folliculorum*, an acarid-like parasite often found in the sebaceous follicles of the face, has been suggested as a possible cause of blepharitis, but it was not recognized in scrapings from the lid margins or in expressed meibomian secretion in any case in this series.

There seems to be no doubt that increased activity of the sebaceous glands of the lid margins predisposes to blepharitis, particularly the seborrheic variety. However, there were a number of clearcut examples of staphylococcic infection of the lid margins in persons with normal skins.

This study has emphasized the importance of routine slit lamp study of the lid margins in all cases of chronic conjunctivitis. When cases of the mild, subclinical form thus uncovered are included, blepharitis, with its associated chronic conjunctivitis, becomes the most common external infection of the eye.

#### SUMMARY AND CONCLUSIONS

1. Blepharitis was the most common external infection of the eye seen in military personnel at this station. In addition to constituting a cosmetic blemish, it was an important cause of ocular disability, both in itself and as a source of conjunctivitis, keratitis and other complica-

tions, causing irritation, blurring of vision due to increased secretion, epiphora, photophobia and eyestain

2 Laboratory and clinical studies of a series of 350 cases indicated that only three important types of blepharitis occurred, namely, staphylococcic blepharitis, seborrheic blepharitis and *Hemophilus duplex* blepharitis. There were many cases of mixed staphylococcic and seborrheic infection. Other causes were unimportant.

3 The three main etiologic types of blepharitis had distinct clinical characteristics and in their pure forms could be differentiated on clinical grounds alone in all but a few cases in which staphylococcic blepharitis simulated *H. duplex* blepharitis.

4 Microscopic examination of scrapings from the lid margins facilitated determination of the etiologic agent. The finding of budding yeast forms, believed to be *Pityrosporum ovale*, was considered a diagnostic sign of seborrheic blepharitis, although its etiologic role in seborrheic dermatitis is still unsettled.

5 Routine biomicroscopic examination of the lid margin in cases of chronic conjunctivitis revealed a high incidence of mild or subclinical blepharitis, which was usually staphylococcic. It is suggested that most cases of chronic conjunctivitis have their origin in blepharitis, which in many instances will escape notice unless magnification is used.

6 Secondary factors in the causation of blepharitis were found to be, in order of their importance: (1) increased activity of the sebaceous and meibomian glands, (2) poor personal hygiene under field conditions of military life and (3) tropical climate, which predisposes to a high incidence of infectious dermatoses. There was no evidence to indicate that vitamin deficiency, refractive error or allergy played significant roles.

## II TREATMENT

A great number and variety of procedures have been advocated for the treatment of blepharitis. Aubaret,<sup>1</sup> in his extensive review, described more than fifty. In this study it was proposed to test and compare the commonly applied procedures and to evaluate them in relation to the etiology, as elucidated in section I. In addition, it was proposed to test the therapeutic efficiency of the new chemotherapeutic agents, particularly sulfathiazole and sulfadiazine, penicillin and tyrothricin. Owing to movements necessarily incident to military personnel, there was a great variation in the time during which treatment could be carried out. Two hundred and sixteen cases, however, were studied therapeutically over a sufficient period of time for conclusions to be drawn from the results.

As indicated in section I, only three important etiologic types of blepharitis were found in this series. These were seborrheic blepharitis,

staphylococcic blepharitis and blepharitis due to *H. duplex*. In addition, there was a large group of cases of mixed staphylococcic and seborrheic infection. The treatment of each of these four groups will be considered separately.

*The Lid Margin as a Skin Structure*—Although blepharitis would seem to be fundamentally a dermatologic problem, there are certain characteristics of the skin of the lid margin which set it apart from the skin of other areas of the body and make it a special therapeutic problem. As is best observed with the slit lamp and corneal microscope, the lid margin is divided into two zones, an anterior zone, containing the cilia, and a posterior zone, containing the orifices of the glands of Zeis and Meibom. The two zones are separated by a fine gray line. The anterior zone, containing the cilia, is entirely cutaneous and can be compared with other hairy areas of the body, such as the brows or scalp, but the posterior zone forms a transitional area between skin and mucous membrane and differs from all similar transitional areas of the body in that it contains the orifices of the meibomian glands. These modified sebaceous glands, which are of unusual length, introduce a unique element into the problem of blepharitis because of their tendency to secretory derangement and their susceptibility to infection. Furthermore, the fact that the lashes are the only hairs on the body which, because of the irritating effect of soap on the eyes, do not participate in the ordinary soap cleansing of the face and scalp further differentiates the lid margins from other comparable structures and has a bearing on the treatment of blepharitis. The proximity of the conjunctiva and cornea, moreover, limits in many respects the type of therapeutic measure which can be employed, since many semi-irritant agents well tolerated by the skin are not at all tolerated by the mucous membranes.

*Treatment of Seborrheic Blepharitis*—There were 52 cases in this series in which the diagnosis was pure seborrheic blepharitis. As previously described in the section on etiology, their most important characteristics were dull, dirty, generally greasy, nonadherent flakes or crusts on the lid margins, with hyperemia and infiltration of the underlying tissues. While a dry type of seborrheic blepharitis has been described and was seen in a few cases, the greasy scaling associated with hypersecretion of the sebaceous glands was present in the vast majority of cases in this series. The condition was never seen without seborrheic dermatitis of the scalp, which appeared in all cases to be the primary focus.

The usual dermatologic treatment of seborrheic dermatitis, as described in modern textbooks of dermatology, follows four main lines:

- 1 Dietetic treatment. Avoidance of alcohol and foods rich in fat, such as butter, peanut butter, pork products, salad oils and fried foods.
- 2 Endocrine treatment. Small doses of thyroid extract for overweight

patients with low basal metabolic rates 3 Local treatment of cutaneous lesions Chief reliance on resorcinol, sulfur, salicylic acid and the mercurial preparations, especially ammoniated mercury 4 Local treatment of the scalp, as the probable primary source Application of agents used on cutaneous lesions, often in combination, and shampoo at least twice a week

An attempt was made to apply these dermatologic procedures to the treatment of seborrheic blepharitis After considerable experimentation, the following routine was worked out 1 Treatment of scalp infection and any other areas of seborrheic dermatitis Most cases were referred to Capt Morris Waisman, M C, chief of the dermatologic section, but occasionally patients with the mild form were treated without consultation by means of biweekly shampoos with liniment of soft soap U S P and biweekly applications of an ointment compounded as follows

|                             |      |
|-----------------------------|------|
|                             | Gm   |
| Ammoniated mercury          | 80   |
| Salicylic acid              | 40   |
| Cetyl alcohol base, to make | 1000 |

2 Local treatment of the lid margins Manual expression of the meibomian glands, careful removal twice a week of scales, sebaceous material and desquamated epithelium by vigorous massage of the lid margins with cotton swabs moistened with solution of boric acid or 1 per cent silver nitrate, application of an ointment, consisting of 1 per cent salicylic acid and 1 per cent yellow mercuric oxide in a petrolatum base, with vigorous massage For home use, the same ointment was prescribed to be used night and morning with gentle massage, the excess ointment to be left on at night but removed in the morning If any symptoms of conjunctivitis were present, a collyrium of a 1 5,000 solution of mercuric oxycyanide was prescribed for use two or three times daily 3 Investigation of dietary habits An attempt was made to correct excesses or other dietary errors

This therapeutic regimen proved to be very successful except for the definite tendency of the condition in many cases to recur This was particularly true of the few cases in which overactivity of the meibomian glands was the most prominent feature In most of these cases the condition recurred as soon as treatment was stopped Recurrences could be minimized, however, by the use of the ointment once or twice a week over an indefinite period

Other methods of treatment which were given a trial included applications to the lid margins two to four times daily of 2 5 per cent ammoniated mercury ointment, 1 per cent resorcinol ointment, 1 or 2 per cent sulfur ointment or 1 per cent sulfur combined with 1 per cent salicylic acid in an ointment base Applications twice weekly of 3 5 per cent tincture of iodine were also tried Acidolate, a water-soluble sul-

fonated oily detergent, was occasionally used for cleansing the lid margin but had the disadvantage of being somewhat irritating to the conjunctiva and cornea. Soaps were also tried for this purpose but proved to be impractical because of the impossibility of limiting their action to the lid margin. None of these procedures was found to have any appreciable advantage over the routine method previously outlined.

A few patients complained of slight irritation from the use of the salicylic acid-yellow mercuric oxide ointment, but in general it was well tolerated. Two cases of sensitivity to mercury were encountered and confirmed by means of patch tests. A typical contact dermatitis occurred, which was relieved by substitution of another medicament for the mercurial ointment.

Treatment of the scalp infection seemed to have a favorable effect on the control of the disease of the lid margins. Reinfection of the lid margins from an active scalp disease by means of the fingers must be considered a possible cause of recurrence.

A group of selected patients with seborrheic blepharitis were treated with the sulfonamide ointments (5 per cent sulfathiazole or 5 per cent sulfadiazine), penicillin ointment and tyrothricin ointment, without effect. Fifteen patients were given large doses of preparations of the vitamin B complex over periods varying from two to six weeks without local treatment of any kind, no obvious change in the infection of the lid margins was observed, and all 15 patients later showed satisfactory response to routine local therapy.

Attempts to improve dietary habits were not altogether satisfactory, owing to the lack of cooperation on the part of some patients and to the difficulty of adjusting diets under military conditions. Only a few patients lived at home, where they could effectively control their diets. In the few who maintained a low fat diet, it was impossible to demonstrate any material decrease in sebaceous activity or any appreciable change in the disease.

*Treatment of Staphylococcic Blepharitis*—As described in the section on etiology, pure staphylococcic blepharitis was found to have clinical characteristics which differentiated it from the other two main etiologic types, seborrheic blepharitis and the form caused by *H. duplex*. The nonulcerative form was characterized by dry, adherent scales on an inflammatory base, and the ulcerative form, by pustules involving the superficial hair follicles and leading to the formation of shallow ulcers. Complications of hordeolum, meibomitis, conjunctivitis and keratitis were common. Of these, meibomitis was the most persistent and troublesome to deal with.

The therapeutic problem in staphylococcic blepharitis revolves on the following necessities: (1) to destroy the bacteria in the lesions, (2) to eliminate or treat predisposing causes, such as seborrhea and

(3) to eliminate other staphylococcic infections of the skin, such as impetigo folliculitis or furunculosis, which could serve to reinfect the lid margins. The main difficulty lies in the destruction of such staphylococci as have gained entrance to the glands of the lid margin, particularly the meibomian glands.

The following groups of therapeutic agents were tested in the 90 cases of staphylococcic blepharitis in this series: (1) antiseptics or germicidal agents not having specific antistaphylococcic action, including silver nitrate, yellow mercuric oxide, ammoniated mercury, mercury bichloride, mercuric oxycyanide, iodine, salicylic acid, merthiolate, zinc sulfate and Quinolol (a mixture of three chlorine derivatives of 8-hydroxyquinoline), (2) dyes, including gentian violet medicinal N N R and brilliant green, (3) sulfonamide drugs, including sulfathiazole and sulfadiazine, (4) antibiotic substances, including penicillin and tyrothricin, and (5) vaccines, including staphylococcus toxoid and stock and autogenous vaccines.

*Tests with Ordinary Antiseptic Drugs*—Application of silver nitrate in 1 or 2 per cent strength to the lid margins, and simultaneously in 0.25 per cent strength without neutralization to the conjunctiva, proved a useful procedure, especially in cases of recent origin. The blackening effect of silver nitrate was prevented by the fact that antiseptic ointments were also used routinely after each application.

After considerable experimentation, the following routine was found to give a satisfactory result in many cases: applications of silver nitrate as just detailed twice a week, combined with applications twice a day of the 1 per cent salicylic acid–1 per cent yellow mercuric oxide ointment to the lid margins, preceded by the instillation of drops of 1:5,000 solution of mercuric oxycyanide into the conjunctival sac. A 2.5 per cent ammoniated mercury ointment was used occasionally as a substitute but appeared to have no advantage over the yellow mercuric oxide–salicylic acid ointment.<sup>14a</sup> With this routine, improvement was obtained in the majority of cases and apparent cure in a considerable number. Other preparations tried included merthiolate (1:5,000) ointment, mercury bichloride (1:3,000) ointment, Quinolol ointment, and 1, 2 and 3.5 per cent tinctures of iodine. No noteworthy results were obtained with any of these preparations except tincture of iodine, which appeared to be very useful, especially in cases of the ulcerative type. It was impossible to use 3.5 per cent tincture of iodine in most cases continuously, however, owing to irritation of the lid margins, but weaker dilutions were well tolerated.

*Test with Brilliant Green and Gentian Violet Medicinal*—A limited number of patients, selected because of failure to respond to other forms of therapy, were tested with these two dyes. Neither preparation could

<sup>14a</sup> Various ointment bases were tested but petrolatum was found to be as satisfactory as any.



be employed routinely because of its disfiguring cosmetic effect, which most patients refused to tolerate. Improvement was obtained in the 4 patients treated with a 2 per cent alcoholic solution of gentian violet medicinal, but it was impossible to follow them long enough to be sure that permanent cures had been achieved.

The brilliant green was applied once daily in a 5 per cent alcoholic solution. It was important to avoid spreading the solution onto the conjunctiva, as it proved to be rather irritating. Fortunately, it was not irritating to the lid margin itself. Five patients to whose lids the dye was applied over periods ranging from two to five weeks were apparently cured but could not be followed long enough for the results to be conclusive. A case of exceptionally severe ulcerative blepharitis of long duration which had resisted all previous treatment is of particular interest. The history follows.

A C., aged 25, had pure staphylococcic blepharitis, which had been present since childhood and was complicated by recurrent ulcerative lesions with loss of cilia and accompanied by moderately severe keratoconjunctivitis. Cultures revealed a hemolytic *Staph aureus*, which was coagulase positive and fermented mannitol and was found to be resistant to both sulfathiazole and penicillin. Previous routine medication had failed, and treatment with sulfathiazole, penicillin, tyrothricin, staphylococcus toxoid, autogenous vaccine and roentgen radiation was ineffective. Over a two year period all methods of therapy proved entirely useless. Brilliant green applied to the lid margins daily produced immediate improvement. The pustules and ulcerations ceased forming immediately and have not recurred over a two month period of observation. Cilia began to reform, and at the time of the last examination only slight hyperemia of the lid margins remained. Cultures yielded no pathogens.

This and other experiences with brilliant green in this series suggest that it is of definite value in the treatment of staphylococcic blepharitis.

*Tests with Sulfathiazole and Sulfadiazine*—These drugs were employed in 5 per cent concentrations in various bases, the commonest being a hydrous wool fat-petrolatum mixture. Vanishing cream bases and other varieties frequently employed on the skin proved to be too irritating for use around the eye. The preparations were used four times daily by preference but in many cases could be used only twice daily.

Both sulfathiazole and sulfadiazine appeared to be much more effective than ordinary antiseptics, and the majority of patients showed satisfactory improvement or healing. A much higher percentage of apparent cures was obtained when the disease was of recent onset than when it was of long duration. The clinical response was usually prompt, as a rule there was demonstrable improvement within four or five days if there was to be any at all. As will be described later, this was also true in penicillin therapy.

Early in the study it was noted that patients without meibomitis responded much more satisfactorily to local sulfonamide therapy than those with it. In the latter event it was necessary to institute supplementary therapy, consisting in manual expression of the glands combined with staphylococcus toxoid or vaccine or both. Although patients whose infection was of recent onset were always benefited by this treatment, patients with long-standing disease were frequently not relieved, even by repeated expressions of the meibomian glands over long periods. That meibomitis was probably the major cause of therapeutic failure in this series is evident from examination of table 4, which lists the results in 216 cases. On clinical grounds it became evident that local chemotherapy with the sulfonamide drugs or with penicillin, even in cases of known strain susceptibility, was not the answer to the problem. The reason for this failure in the case of penicillin therapy was shown experimentally in 2 cases to be due to failure of the drug to penetrate

TABLE 4—Results of Treatment in 216 Cases of Blepharitis\*

|   | Slight or No<br>Improvement | Improvement | Healing |
|---|-----------------------------|-------------|---------|
| Seborrheic blepharitis                          | 2                           | 24          | 26      |
| Staphylococcal blepharitis                      |                             |             |         |
| Without meibomitis                              | 2                           | 38          | 30      |
| With meibomitis                                 | 6                           | 13          | 1       |
| Blepharitis due to <i>Hemophilus duplex</i>     | 0                           | 0           | 4       |
| Mixed seborrheic and staphylococcal blepharitis |                             |             |         |
| Without meibomitis                              | 2                           | 37          | 11      |
| With meibomitis                                 | 3                           | 16          | 1       |

\* Treatment time at least three weeks

the meibomian glands after it had been applied to the lid margin repeatedly. Nor could penicillin be demonstrated in expressed secretion from the meibomian glands in 2 cases in which a full therapeutic dose was given by the intramuscular route.

In 4 cases sensitization to sulfathiazole was observed during the course of treatment. In 2 of these cases there was a history of previous oral therapy with sulfathiazole which had been followed by cutaneous eruptions. No sensitivity to sulfadiazine was observed. In order to minimize the possibility of drug sensitization, the period of treatment for the sulfonamide drugs was limited to seven days.

The effect of oral sulfadiazine therapy on staphylococcal blepharitis was observed in 4 cases in which treatment was being given for infection of the respiratory tract. It is noteworthy that no permanent improvement occurred in any of them.

*Tests with Penicillin and Tyrothricin*—Penicillin was employed in 87 cases. The routine method of application was in solution form (500 units per cubic centimeter) and as an ointment (1,000 units per gram

in a petrolatum or a petrolatum-hydrous wool fat base) The drops were instilled four times daily, and the ointment was applied night and morning In certain test cases the ointment alone was used every hour during the waking hours Penicillin sensitivity tests were performed on each culture (table 5), but the penicillin was employed irrespective of the results of the tests in order to obtain data as to their clinical value

TABLE 5—*Penicillin Sensitivity of 98 Strains of Pathogenic Staphylococci*

| Strain Sensitivity,<br>Oxford Units<br>per Cc | No of<br>Strains | Strain Sensitivity,<br>Oxford Units<br>per Cc | No of<br>Strains |
|---|------------------|---|------------------|
| Inhibited by                                  |                  | Inhibited by                                  |                  |
| 0.005   | 1                | 0.32  | 5                |
| 0.01  | 2                | 1.0   | 5                |
| 0.02  | 16               | 5.0   | 1                |
| 0.04  | 23               |   |                  |
| 0.05  | 3                | Not inhibited by                              |                  |
| 0.08  | 11               | 5.0   | 25               |
| 0.15  | 5                | 500.0   | 1                |

TABLE 6—*Correlation of Penicillin Sensitivity and Clinical Response in 48 Cases of Staphylococcic Blepharitis*

| Strain Sensitivity,<br>Oxford Units per Cc | No Improvement | Improvement | Healing |
|--|----------------|-------------|---------|
| Inhibited by                               |                |             |         |
| 0.01                                       | 1              |             |         |
| 0.02                                       | 1              | 6           | 1       |
| 0.04                                       | 2              | 8           | 2       |
| 0.05                                       | 1              | 1           |         |
| 0.08                                       |                | 2           | 5       |
| 0.16                                       |                | 1           |         |
| 0.32                                       |                | 1           |         |
| Not inhibited by                           |                |             |         |
| 5.0  | 14             | 1           |         |
| 500.0                                      | 1              |             |         |

TABLE 7—*Clinical Response to Penicillin Therapy in 43 Cases of Staphylococcic Blepharitis*

| No Change | Improvement | Healing |
|-----------|-------------|---------|
| 6         | 24          | 13      |

\* Penicillin sensitivity not known

Penicillin proved to be moderately effective (tables 6 and 7) in relieving the symptoms of staphylococcic blepharitis, but the results still left something to be desired In a few instances clinical cure without relapse was obtained in as short a time as a week, but in general relapses were frequent, and in some cases the condition proved completely resistant

Two special bases were employed in an effort to obtain greater release of the penicillin into the tissues, but clinical results with these preparations were not noticeably better than with the others

In 4 cases sensitivity to penicillin developed during therapy. Typical contact dermatitis developed, and positive reactions to patch tests were obtained. As will be seen in table 6, there was a definite correlation between penicillin sensitivity in vitro and clinical response to penicillin therapy. Response usually became apparent within forty-eight hours if it was to occur at all.

Tyrothricin was employed in only 14 cases, owing to the necessity of purchasing it privately. The cases were partially selected in that only those were used in which the disease had resisted ordinary methods of therapy. The drug was applied in the form of drops (33 mg per hundred cubic centimeters) and ointment (50 mg per hundred grams) exactly as in the case of penicillin. In 6 of the 14 cases there was pronounced improvement, but the condition in the rest was unchanged. In the concentrations employed the drug was not irritating to the conjunctiva or the lid margins. In view of the partial success obtained, it is believed that this method of treatment deserves further study.

*Tests with Staphylococcus Toxoid and Vaccines*—Previous studies by Murray<sup>15</sup> and by me<sup>16</sup> indicated that staphylococcus toxoid was of value in the treatment of staphylococcic blepharitis which had resisted ordinary methods of treatment. This was denied in a report by Julianelle, Boots and Harrison<sup>17</sup> but was apparently confirmed in a series of studies by Allen<sup>18</sup>. Pathogenic staphylococci are known to elaborate exotoxins capable of producing severe inflammation when instilled into the conjunctival sac or injected into the skin. The rationale for the use of toxoid to induce antitoxic immunity is therefore clear. At the same time, it must be realized that pathogenic staphylococci also have endotoxins, which appear to be concerned with the organism's invasiveness. Their presence forms the rationale for the use of vaccines, either stock or autogenous.

In this series staphylococcic toxoid was administered in 55 cases, but in only 27 cases was the full course given. Only in cases of blepharitis which was complicated by meibomitis or by severe conjunctivitis or keratitis or in cases in which the condition had resisted routine treatment was toxoid therapy given. It was used as a supplementary measure only, local treatment being continued in every case. It was not possible in mixed therapy of this type to appraise the value of the toxoid injection.

15 Murray, D. S., and Glasg, M. B. *Staphylococcus Toxoid*, *Lancet* **1** 303 (Feb. 9) 1935, cited by Julianelle, Boots and Harrison<sup>17</sup>.

16 Thygeson, P. *Treatment of Staphylococcic Blepharoconjunctivitis with Staphylococcus Toxoid*, *Arch. Ophth.* **26** 430 (Sept.) 1941.

17 Julianelle, L. A., Boots, R. H., and Harrison, G. H. *The Treatment of Staphylococcal Infections of the Eye by Immunization with Toxoid*, *Am. J. Ophth.* **25** 431 (April) 1942.

18 Allen, J. H., in discussion on Thygeson<sup>16</sup>.

tions, but the general impression gained was that they were of distinct value. The few patients who showed extensive cutaneous reactions to intradermal injections of the toxoid improved more rapidly than those with minimal or negative cutaneous reactions.

Only 1 patient was treated with a staphylococcus toxoid combined with stock vaccine. This patient had a severe staphylococcic blepharitis, complicated with meibomitis, conjunctivitis and keratitis, which was totally resistant to local therapy, including applications of sulfathiazole ointment and penicillin. During a course of treatments with the toxoid the keratitis disappeared and the conjunctivitis improved although pathogenic staphylococci persisted on the lid margin.

Stock vaccine was used in only 8 cases and autogenous vaccine in only 1. These vaccines were used in conjunction with staphylococcus toxoid in all 9 cases, so that, although the blepharitis improved in 8 cases during and after therapy, it was impossible to evaluate the results.

*Treatment of Blepharitis Due to H. Duplex*—In the 4 cases of uncomplicated blepharitis due to *H. duplex* in this series healing was rapid after short periods of treatment with sulfathiazole ointment used four times daily. No recurrences were noted. The classic treatment with zinc sulfate in the form of drops and ointment has been equally effective in cases I have seen in the civilian population unless there was mixed infection with staphylococci.

*Treatment of Mixed Seborrhic and Staphylococcic Blepharitis*—Cases of this common type of blepharitis presented the most difficult therapeutic problem of the series. The results obtained in treatment were definitely inferior to those obtained with either the pure seborrhic or the pure staphylococcic disease.

After considerable experimentation, it was found that the seborrhic factor was best treated first. This was done by the same methods as those employed in treating pure seborrhic blepharitis, particular attention being given to the meibomian glands, which were expressed frequently. The most satisfactory local treatment appeared to be applications of the 1 per cent yellow mercuric oxide–1 per cent salicylic acid ointment. Again, scrapings from the lid margin were used as a guide to therapy. After the slides became negative for *P. ovale*, a course of treatments with sulfathiazole or penicillin ointment was prescribed, and when meibomitis was present staphylococcus toxoid was employed. Under this regimen, satisfactory clinical improvement was obtained in most cases and clinical cures in a moderate percentage.

Other treatments employed, including use of tincture of iodine, sulfur and resorcinol, offered no appreciable advantages.

The importance of keeping the scalp and other areas of the skin free from active seborrhic dermatitis was evident in numerous cases.

in this group in which involvement of the lid margins recurred repeatedly until infection of the scalp was controlled

*Treatment of Secondary Conjunctivitis and Keratitis*—In cases of pure seborrheic blepharitis, conjunctivitis was an infrequent complication and was readily controlled by the use of mild antiseptics, such as 0.25 per cent silver nitrate combined with a collyrium of a 1:5,000 solution of mercuric oxycyanide, used two or three times daily. There were no corneal complications.

In cases of pure staphylococcic blepharitis, conjunctivitis and keratitis were serious complications. The conjunctivitis varied from a mild catarrhal type to a severe form with copious mucopurulent exudate and intense cellular infiltration of the membrane. The corneal complications also varied from superficial epithelial keratitis with punctate erosions, staining with fluorescein, located most prominently in the lower portions of the cornea, to fulminating keratitis with multiple corneal infiltrations and ulcers. In all these cases it was obvious that treatment of the lid margins was of first importance and conjunctival treatment of secondary importance. In none of the cases of corneal involvement was it necessary to treat the cornea directly by chemical or actual cautery. All methods of antistaphylococcic treatment described for blepharitis were effective in these cases, but sulfathiazole and penicillin were superior to the ordinary antiseptics. The use of staphylococcus toxoid was particularly valuable in the treatment of the corneal complications, especially the superficial keratitis with punctate epithelial erosions.

In cases of mixed seborrheic and staphylococcic blepharitis the conjunctivitis and keratitis were also serious complications but differed in no important way, except in resistance to treatment, from the complications occurring with pure staphylococcic blepharitis. In all types of staphylococcic conjunctivitis and keratitis the primary role of the infection of the lid margin was obvious.

As is always true, conjunctivitis due to *H. duplex* accompanied the blepharitis caused by the same organism in the cases in this series and responded well to sulfathiazole ointment. It has been seen to respond equally well to zinc sulfate in cases in the civilian population.

#### COMMENT

The treatment of blepharitis, other than the type due to *H. duplex*, which is no problem, cannot be said to be wholly satisfactory at present. Although the majority of patients can be relieved under ideal conditions, there is one inescapable factor which militates against permanent cure, treatment with present methods is at best a long-drawn-out affair, and even at a military post, where cure is free and the time lost in reporting to the clinic is at government expense, certain patients will not cooperate for the required length of time. Under civilian conditions failure to

complete the course occurs much more frequently. It is clear that future control of the disease will depend largely on the development of measures which will be effective in days or weeks, rather than in months. The recent advances in chemotherapy appear to offer only a partial solution to the problem.

From this study it is apparent that infection of the meibomian glands is the greatest single factor which must be overcome. Meibomitis was present in all cases in which the blepharitis was resistant to therapy, and methods of treating it were obviously inadequate. Repeated expression of the glands was a useful procedure and in some instances resulted in apparent cure. In general, however, expression was only palliative. The inability of both general and topical chemotherapy with the sulfonamide drugs and with penicillin to affect the condition was also made clear in this series. In the case of penicillin at least, it was shown experimentally that the drug failed to enter the secretions of the meibomian glands in demonstrable amounts after local and intramuscular therapy, and the finding was confirmed clinically by the fact that penicillin-sensitive organisms were cultured from these secretions during the course of both types of treatment. In this connection, it is of interest to report a case of internal hordeolum which developed in a patient receiving 100,000 units of penicillin daily. The strain of staphylococcus recovered from the hordeolum was fully sensitive to penicillin. Hypersecretion of the meibomian glands, with dilatation of their orifices, appeared to be the main factor in their susceptibility to infection. No satisfactory means of reducing this hypersecretion is at present known. In selected cases in this series reduction of fats in the diet had no noticeable effect on it.

In view of the minimal clinical symptoms incident to pure seborrheic blepharitis, it is apparent that its principal importance lies in its role of providing a suitable soil for the growth of pathogenic staphylococci. The chief problem is the matter of recurrence. The importance of treating the primary focus, the scalp, which is stressed in all textbooks of dermatology, was amply confirmed in this study, for, although it was impossible to say positively that recurrences were due to reinfection, the general impression was gained that reinfection from the scalp was common.

Assuming that *P. ovale* is the cause of the disease, the fungicidal effect of all the agents used in this series, including tincture of iodine, silver nitrate, salicylic acid, ammoniated mercury and yellow mercuric oxide, was evident from examination of scrapings from the lid margins, which were negative for the yeast after treatment. The failure of penicillin or of sulfathiazole to influence the condition is in accordance with the known fact that these drugs fail to affect mycotic infections.

The recent dermatologic literature has been full of reports<sup>19</sup> criticizing topical applications of the sulfonamide drugs because of the high incidence of allergic reactions. The danger of sensitization has appeared to outweigh the benefit to be obtained from local therapy. The results in this series, however, would seem to indicate that sulfathiazole and sulfadiazine can be used for topical application around the eyes with minimal danger, since only 4 cases of sensitization occurred in the group of over 300 patients treated, in 2 of the 4 cases, moreover, sensitization was clearly related to previous oral use of the drug. No sensitivity to sulfadiazine developed in any of the 60 cases in which it was employed. Long-continued use of the sulfonamide drugs in treatment of blepharitis, however, would seem to be not only unwise but unnecessary, for if there is to be any clinical response to the drug it will occur within fifteen days, at the longest.

Sensitization to penicillin (or possibly to impurities contained in it) occurred in 5 cases in a considerably smaller series, and in my opinion was of more significance than the allergic reactions to sulfathiazole. There is no adequate substitute for penicillin at the present time, so that sensitization could be a serious matter in the event that general penicillin therapy was later needed. On the other hand, since cross sensitization among the sulfonamide compounds is not common, sensitivity to sulfathiazole does not necessarily preclude all subsequent sulfonamide therapy. For this reason, it is recommended that topical use of penicillin be reserved for those cases in which the disease has failed to respond to other medication and that its administration be limited to not more than ten days.

In this series the only instances of "overtreatment dermatitis" observed were 3 cases in which daily applications of 3.5 per cent iodine were used. The condition was readily recognized and treatment discontinued. The possibility of the deleterious effect of overtreatment was considered at all times, and frequent rest periods, as well as rotation of procedures, were employed in cases of long-drawn-out treatment for the purpose of detecting it.

Several cases of severe keratitis accompanying blepharitis appeared to be related to insufficient closure of the lids while sleeping. It was possible to obtain observations on the patients during sleep and to show that they did not have normal closure of the lids. Other patients with blepharitis, however, had the same symptom but no keratitis. It is probable, therefore, that the keratitis was primarily staphylococcal in origin and was aggravated, rather than caused, by the drying effect of incomplete closure of the lids.

<sup>19</sup> Cole, H. N. The Local Use of Sulfonamide Compounds in Dermatology, J. A. M. A. **123** 411 (Oct 16) 1943.



In this series patients with well established blepharitis in general exhibited a genuine desire to be cured and were extraordinarily faithful in reporting to the clinic for treatment. Careful questioning, however, revealed that they were not so faithful in the daily use of their medications. As their conditions improved, they became more and more careless about treating themselves. The relative efficacy of clinic versus home treatment was well illustrated in a series of 15 consecutive patients who were available for daily treatment. Improvement was much more striking than in patients who could be treated only once or twice a week.

#### SUMMARY AND CONCLUSIONS

A large series of cases of blepharitis among military personnel were subjected to therapeutic study with the following five groups of medications: (1) antiseptic or germicidal drugs, including silver nitrate, zinc sulfate, yellow mercuric oxide, ammoniated mercury, mercuric oxycyanide, mercury bichloride, tincture of iodine, salicylic acid, sulfur, resorcinol, Quinolol and merthiolate, (2) dyes, including gentian violet medicinal, N N R and brilliant green, (3) sulfonamide drugs, including sulfathiazole and sulfadiazine, (4) antibiotic substances, including penicillin and tryothricin, and (5) vaccines, including staphylococcus toxoid, toxoid combined with vaccine and stock and autogenous vaccines.

Seborrheic blepharitis responded best to the following treatment: (1) daily mechanical cleansing of the lid margins, (2) frequent expression of the meibomian glands, (3) applications of 0.25 per cent solution of silver nitrate to the conjunctiva and 1 per cent silver nitrate to the lid margins twice weekly, (4) applications twice daily of an ointment containing 1 per cent yellow mercuric oxide and 1 per cent salicylic acid to the lid margins, and (5) treatment of associated seborrheic dermatitis of the scalp, brows and external ears. Sulfathiazole and penicillin applied in ointment form were ineffective.

Staphylococcal blepharitis responded well to topical treatment with the following preparations, listed in order of efficacy, penicillin, sulfathiazole or sulfadiazine, and mercurial preparations, including ammoniated mercury ointment and a combination of 1 per cent yellow mercuric oxide and 1 per cent salicylic acid in a petrolatum base. Administration of staphylococcus toxoid proved to be an important supplementary procedure. Other measures of therapeutic value included topical application of tincture of iodine, gentian violet medicinal and brilliant green to the lid margins. Treatment of other staphylococcal infections of the face or scalp was important.

In cases of staphylococcal blepharitis a close correlation between the sensitivity of the strain of staphylococcus to penicillin and the clinical response of the disease to topical penicillin therapy was noted.

Staphylococcic blepharitis complicated by meibomitis was much more resistant to therapy than uncomplicated blepharitis

Blepharitis due to *Hemophilus duplex*, of which 4 cases occurred, responded completely and rapidly to topical application of sulfathiazole in ointment form

Mixed seborrheic and staphylococcic blepharitis proved to be more resistant to therapy than either form alone. It was found best to treat the seborrheic factor first and to give particular attention to expression of the meibomian glands. After scrapings from the lid margins had become negative for *P. ovale*, antistaphylococcic treatment with sulfathiazole or penicillin ointment was employed. *Staphylococcus toxoid* was a valuable supplementary treatment.

Contact dermatitis as a result of allergy to both penicillin and sulfathiazole was observed but did not occur often enough to prejudice their use.

In pure seborrheic blepharitis, conjunctivitis was an infrequent complication and was readily controlled by the use of mild antiseptics; there were no corneal complications. In pure and mixed staphylococcic blepharitis, conjunctivitis and keratitis were serious complications, requiring conjunctival treatment with antistaphylococcic agents. The importance of the infection of the lid margins as the primary focus was obvious in all cases.

While local chemotherapy with the sulfonamide drugs and with penicillin constitutes a great advance in the treatment of staphylococcic blepharitis, the results in this series indicate that therapy is still not entirely satisfactory, especially in cases complicated with meibomitis.

Adequate treatment of blepharitis is of distinct military importance both for the removal of local irritation and for the prevention of serious corneal complications.

Major Alfred M. Glazer, M.C., chief of the laboratory service, placed all laboratory facilities at my disposal, and Capt. Joseph S. Gots, S.C., bacteriologist, and his technicians made the culture studies. Capt. Morris Waisman, M.C., chief of the section of dermatology, served as dermatologic consultant, and my associates, Major S. R. Irvine, M.C., and Capt. Joseph W. Hallett, M.C. aided in the clinical study.

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# RETROBULBAR NEURITIS AND COMPLETE HEART BLOCK CAUSED BY DIGITALIS POISONING

Report of a Case

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ALTHOUGH disturbances of vision resulting from digitalis intoxication have been described in many forms and by many investigators, no definite instance of retrobulbar neuritis caused by digitalis poisoning appears to have been reported in the literature. Recently, Carroll<sup>1</sup> reported 6 cases of colored vision caused by digitalis intoxication. No defects in the visual fields were present in these cases. In a discussion of his own paper,<sup>2</sup> he mentioned that Dr D F Gillette, of Syracuse, N Y, had observed 2 cases of retrobulbar neuritis resulting from digitalis poisoning. These cases, as yet, have not been reported in the literature.

Colored vision is a rather common visual manifestation of digitalis poisoning. The chromatopsia is most common for yellow or green, but red, brown, blue or white vision has been described.<sup>3</sup> Langdon and

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From the Section on Ophthalmology (Dr Wagener) and the Section on Medicine (Dr Smith), the Mayo Clinic

1 Carroll, F D. Visual Symptoms Caused by Digitalis, *Am J Ophth* **28** 373-376 (April) 1945

2 Carroll, F D, in discussion on Carroll, F D. Visual Symptoms Caused by Digitalis, *Arch Ophth* **34** 166 (Aug) 1945

3 (a) Carroll<sup>1</sup> (b) Chamberlain, E C. Digitalis Poisoning, *J Florida M A* **28** 586-588 (June) 1942 (c) Giesler, F, and Wolff, K. Beitrag zur Xanthopsie nach Digitalis, *Klin Monatsbl f Augenh* **79** 203-208 (Sept 2) 1927 (d) Langdon, H M, and Mulberger, R D. Visual Disturbance After Ingestion of Digitalis, *Am J Ophth* **28** 639-640 (June) 1945 (e) Robey, W H. Visual Disturbances with Digitalis Medication, *New England J Med* **213** 248-251 (Aug 8) 1935 (f) Smith, H L J. Digitalis Delirium with Colored Vision. Report of One Case, *J Iowa M Soc* **21** 173-174 (April) 1931 (g) Sprague, H B, White, P D, and Kellogg, J F. Disturbances of Vision Due to Digitalis, *J A M A* **85** 716-719 (Sept 5) 1925 (h) Willius, F A. Cardiac Clinics, Digitalis Poisoning with Cerebral Symptoms, Coronary Sclerosis with Angina Pectoris, and Paroxysmal Dyspnea, *Proc Staff Meet, Mayo Clin* **10** 649-653 (Oct 9) 1935

Mulberger<sup>3d</sup> stated that a relative central scotoma was present in case 4 of their series, but they intimated later that a marked change in refraction accounted for the blurring of vision. In several reports frosted or snowy vision has been noted.<sup>4</sup> Flickering sensations before the eyes also have been described, first by Purkinje, who used himself as a test subject and recorded the toxic manifestations.<sup>5</sup> "A peculiar oscillating movement of the eyes" was described by Galentine<sup>6</sup> in the case of an 8 or 9 year old boy, who recovered completely in a few days after withdrawal of the digitalis. Blurring of vision has been noted many times, and 1 case of temporary complete blindness was reported in the literature<sup>7</sup>, but in few cases has the visual acuity been recorded and the visual fields plotted. Some authors<sup>8</sup> have specifically made note of the absence of defects in the visual fields, but the rest either were unable to make perimetric studies or neglected to report the absence of field defects.

Carroll<sup>1</sup> postulated

the confused vision is due to central functional impairment which, in turn, is due to the drug. The temporary complete blindness mentioned in the literature probably was due to the cerebral intoxication, that is, a cortical type of blindness was induced which disappeared on stopping the drug.

This conception, namely, a central intoxication, has been generally accepted as the cause of the visual disturbances associated with digitalis poisoning. The purpose of this paper is to demonstrate that digitalis poisoning can affect not only the higher cerebral centers but also the papillomacular fibers of the optic nerve. Digitalis has a selective action on the vagus nerves, the auriculoventricular conduction mechanism and

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4 Carroll<sup>1</sup> Langdon and Mulberger<sup>3d</sup>

5 Hanzlik, P. J. Jan Evangelista Purkyně (Purkinje) on Disturbances of the Vision by Digitalis, One Hundred Years Ago, *J. A. M. A.* **84** 2024-2025 (June 27) 1925

6 Galentine, C. B. Cumulative Effects of Digitalis, *Boston M. & S. J.* **49** 205-206, 1854

7 (a) Langdon and Mulberger<sup>3d</sup> (b) Sprague, White and Kellogg<sup>3g</sup> (c) Adams, P., in discussion on Gunn, J. A. Toxic Amblyopia, *Tr. Ophth. Soc. U. Kingdom* **50** 396, 1930 (d) Berger, E. H. Digitalis Intoxication, *Northwest Med.* **32** 195-196 (May) 1933 (e) Carr, J. G. Digitalis Delirium, *M. Clin. North America* **9** 1391-1398 (March) 1926 (f) Edward, J. On a Case of Poisoning by the Root of Digitalis Purpurea, *Lancet* **2** 31-32 (July 14) 1849 (g) Jackson, H., Jr., and Zervas, L. G. A Case of Yellow Vision Associated with Digitalis Poisoning, *Boston M. & S. J.* **192** 890-893 (May 7) 1925 (h) Parson, G. W. The Visual and Cerebral Manifestations of Digitalis Intoxication. Case Report, *Tri-State M. J.* **7** 1375-1376 (Nov.) 1934

8 Carroll<sup>1</sup> Giesler and Wolff<sup>3c</sup> Adams<sup>7c</sup>

the sinoauricular node<sup>9</sup> Hence, it is not incorrect to postulate the possibility of direct damage to the optic nerves secondary to generalized systemic intoxication Weiss,<sup>10</sup> in discussing the effects of digitalis on the central nervous system, concluded that the yellow vision, which is frequently encountered, is due to disturbance of centers in the medulla and the midbrain, similar to the primary disturbance in function of the vagus nerve, which is the desired effect of the drug Giesler and Wolff<sup>11</sup> concluded that damage to the retrobulbar portion of the optic nerve caused the xanthopsia in their case, but they also mentioned the possibility of changes occurring in the refracting media, such as those seen with jaundice, and of cortical damage In their case examination of the perimetric fields did not disclose any central defects but revealed loss of ability to recognize blue targets throughout the field

Since digitalis is in constant and universal use today, and will continue to be used, its toxic manifestations cannot be overemphasized Berger<sup>12</sup> and Edward<sup>13</sup> have both reported cases of fatal digitalis poisoning, hence, knowledge of its early toxic effects is of extreme value It is significant to note that in the case reported by Giesler and Wolff the offending drug was not digitalis leaf, but gitalin, one of its glucosides<sup>14</sup> Smith<sup>15</sup> said that older persons, particularly those having arteriosclerosis, do not tolerate digitalis as well as younger patients and must be more closely observed for, and questioned about, the onset of toxic manifestations

#### REPORT OF CASE

A white man aged 50 registered at the Mayo Clinic on April 2, 1945 because of poor vision, generalized weakness, nausea and vomiting Two or three months previously he had had extrasystoles and had been given "leaf medicine," 1 tablet four times daily for about two weeks After two weeks his medicine had been changed to another "green digitalis tablet", he had taken 1 tablet three times daily for six weeks About two weeks before he came to the clinic his appetite had become poor, he had vomited several times and had had diarrhea, which had alternated with constipation At the same time he had noticed that lights had become yellow and that green grass had assumed a yellow tint His vision had also become blurred, and he had found himself unable to read His local oculist had been unable to determine the cause of the blurred vision and, on finding blurring of the margins of the optic disks, suggesting increased intracranial pressure, had advised the patient to seek further advice

9 Goodman, L, and Gilman, A The Pharmacological Basis of Therapeutics, New York, The Macmillan Company, 1941, p 505

10 Weiss, S The Effects of the Digitalis Bodies on the Nervous System An Analysis of the Mechanism of Cardiac Slowing, Nausea, and Vomiting, Psychosis, and Visual Disturbance Following Digitalis Therapy, *M Clin North America* **15** 963-982 (Jan) 1932

11 Smith, H L Cerebral Manifestations of Digitalis Intoxication, *Proc Staff Meet, Mayo Clin* **13** 574-575 (Sept 7) 1938

The blood pressure was 138 mm of mercury systolic and 78 mm diastolic. The pulse rate was 60 beats per minute, and the rhythm was regular. The heart was normal in size, and no significant murmurs were present. The abdomen was essentially normal except for bilateral inguinal hernia, for which the patient wore a truss. The prostate gland was moderately enlarged. The central nervous system was normal.

Corrected vision was 6/60 and 14/178 in the right eye and 6/60 and 14/224 in the left eye. Externally the eyes were normal. There was no imbalance of the ocular muscles, and the peripheral visual fields were full when tested by the confrontation method. The ocular fundi were essentially normal. The optic disks were flat, there were some thickening of the scleral rings and slight astigmatic blurring of the outlines of the disks. A few hyaline spots were present in the macular choroid of each eye. No gross vascular lesions were seen in the fundi. The central visual fields were plotted on the tangent screen at a distance of 1 meter (fig 1). The field of each eye contained an 8 degree relative central

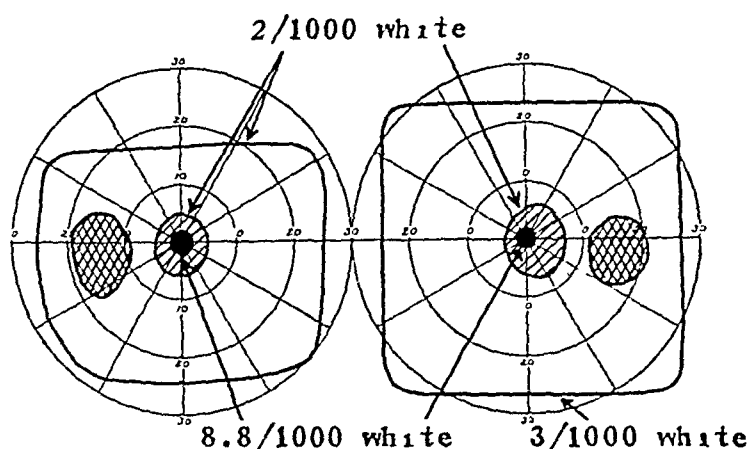


Fig 1—Central scotoma in the field of each eye, taken April 2, 1945 with a tangent screen at a distance of 1 meter, showing density to a 8.8 mm white target. The blindspots are slightly enlarged. Vision was 6/60 and 14/224 in the left eye and 6/60 and 14/178 in the right eye, with correction.

scotoma for a 2 mm white bead. A small central focus in each scotoma was dense to an 8.8 mm white target and to a red test object of the same size. Blue was not recognized in any part of either field. The physiologic blindspots were slightly larger than normal.

An electrocardiogram made on April 3, 1945 (fig 2 A) revealed a rate of 58, intermittent delayed auriculoventricular conduction and complete heart block, left axis deviation, slurring of the QRS complex in leads I and II, diphasic T waves in leads I and III and inversion of the T waves in lead III and diphasic T waves and depression of the S-T segments in the two precordial leads ( $CR_2$  and  $CR_3$ ). A flocculation test for syphilis gave negative results. The value for the hemoglobin was 11.7 Gm per hundred cubic centimeters of blood, the erythrocyte count was 5,050,000, and the leukocyte count 14,600, per cubic millimeter of blood. Routine urinalysis did not reveal any abnormality. Roentgenologic examination of the thorax disclosed a Ghon complex on the left side. Roentgenograms of the head revealed calcification of the falx cerebri and slight hyperostosis of the right frontal bone.

The diagnosis was digitalis intoxication with complete heart block and toxic amblyopia due to retrobulbar optic neuritis. The administration of digitalis was discontinued, and increasing amounts of fluids were administered orally. The patient remained at the clinic for one week. During this time he was observed several times, the central visual fields were examined, and electrocardiograms were made. The visual acuity improved gradually, on April 9 the vision was 6/12 and 14/21 in the right eye and 6/10 and 14/21 in the left eye, with a +2.00 D lens added for near vision.

On the tangent screen at a distance of 1 meter there was in the field of each eye an 8 degree residual central scotoma for a 1 mm white target. Within each central scotoma there was a small temporal paracentral scotoma, dense to a 3 mm white target in the right eye and to a 2 mm white target in the left eye.

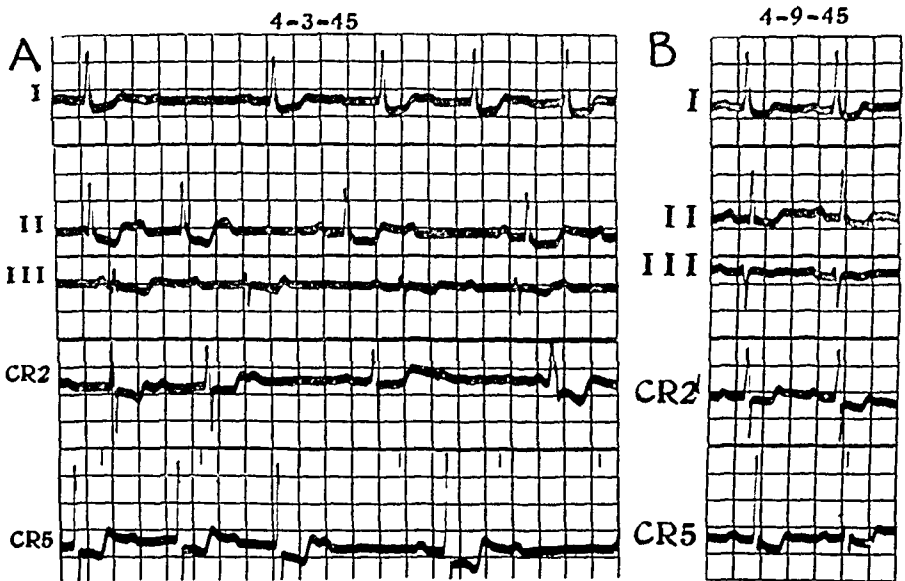


Fig 2—*A*, electrocardiogram made April 3, 1945, showing a rate of 58, intermittent delayed auriculoventricular conduction and complete heart block, left axis deviation, slurring of the QRS complex in leads I and II, diphasic T waves in leads I and III and inversion of the T waves in lead III, and diphasic T waves and depression of the S-T segments in the two precordial leads ( $CR_2$  and  $CR_5$ ).

*B*, electrocardiogram made April 9, 1945, showing a rate of 90, sinus tachycardia, slurring of the QRS complex in leads I and III, left axis deviation, diphasic T waves in leads I and II and inversion of the T waves in lead III, and diphasic T waves and slight depression of the S-T segments in the two precordial leads ( $CR_2$  and  $CR_5$ ).

An electrocardiogram made on April 9, 1945 (fig 2 *B*) showed a rate of 90, sinus tachycardia, slurring of the QRS complex in leads I and III, left axis deviation, diphasic T waves in leads I and II and inversion of the T waves in lead III, and diphasic T waves and slight depression of the S-T segments in the two precordial leads ( $CR_2$  and  $CR_5$ ).

One month after his dismissal from the clinic, the patient reported by letter that his eyes and general physical condition had returned to normal.

## COMMENT

In most cases of digitalis intoxication with disturbances of color vision the patients are hospitalized and are too ill to permit mapping of the perimetric and the tangent screen fields. Often, disorientation prevents even the gross determination of the visual acuity. When this can be determined with the use of bedside reading charts, it often is found to be considerably reduced, and when the fields appear to be normal with the gross confrontation test, the presence of central scotomas may be logically suspected. In the present case, it was fortunate that the patient's physical and mental condition was sufficiently good to permit the definite demonstration of bilateral central scotomatous defects in the fields of vision, although it was not possible to make complete perimetric studies. The vision returned to normal in about five weeks without treatment except for withdrawal of the digitalis and increasing the amount of fluid ingested by mouth.

The Mayo Clinic



## EXPOSURE AND FIXATION OF THE EYE IN THE EARLY DAYS OF CATARACT EXTRACTION

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OPHTHALMOLOGY, which might be likened to a highly specialized organ in the "body medical," has been characterized by an unflinching tendency to absorb into itself with imperious force whatever good might come within its grasp, while rejecting from its constitution all empiric elements which might have affected its vitality and, so to speak, metabolically, hindered the development of a creature which has, in time, influenced all medicine and led to the happiness of the world. It should be profitable for us as ophthalmologists, in this fiftieth century since the earliest recordings, to remind ourselves that this development has been but slowly progressive and that the hidden forces within the body were derived usually from single inventions or observations.

Today the tyro is inclined to accept the present status as he finds it, oblivious of how laboriously the science has struggled to attain its, so great, stature. He accepts as matters of course many conditions now existing, and the practice of numerous technical procedures, just as though they had existed from the most primitive times, unaware of their obscure and halting beginnings.

Although I have been in practice many years, the extraction of cataract is as thrilling to me today as when I saw the operation for the first time. Constantly, my mind goes back to that event and asks, "What was the beginning of cataract operations like?" And, as I have observed the ease with which my young assistants have approached their vital cases, employing but few, simple instruments, I am reminded that once upon a time those instruments had not yet been devised to take the place of earlier, complicated and cumbersome implements.

Much has been changed in my own time. I recall my beginnings at Wills Hospital. One of my duties was the selection and preparation of instruments in time for the surgeons' visits in the afternoons. For one surgeon, the racks in each of the small metal trays should hold thirteen, for another, seventeen. Certain operators wished to have duplicates, handy to meet any emergency, yet, commonly, the most skilful might use only seven!

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Read at the Eighty-First Annual Meeting of the American Ophthalmological Society, Hot Springs, Va., Nov. 11, 1945

Several years ago, while I was perusing Baron Wenzel's "Treatise on Cataract,"<sup>1</sup> as translated from the French, in 1791, my eye caught this sentence "It is most extraordinary that amongst the eminent persons who have described the operation of extracting the cataract most of them have enumerated amongst its principal difficulties the quick and convulsive action of the eye, and that they should have taken such pains to contrive instruments for the purpose of fixing it" And, "There are some who still employ Specula, to fix the eye, notwithstanding the mischievous effects these always produce" And, again, "Why, from mere love of innovation, are new instruments continually introduced, which fall short of the boasted advantages attributed to them by their inventors?" "These admonitions," the Baron declares, he advances "only to describe and justify the teachings of his father," that famous peripatetic oculist who had gone about the Continent couching cataracts, on rich and poor, with great and variable success

Having performed many extractions myself, I have witnessed uncounted numbers by the hands of "eminent persons," who but rarely enumerated, among the principal difficulties, the "quick and convulsive motion of the eye," although all had constantly "fixed the eyes" with instruments contrived for that purpose

In the light of achievements and facilities, my thoughts run back to remoter times, causing me to wonder how old time surgeons exposed the globe to enable them to view the operative field and how they fixed the globe in order to prevent "convulsive motion"

Teacher Collins, while recounting incidents during his early days at Moorfields, told me that one of the surgeons, whose technic was the wonder of every visitor who came to the hospital, would allow the nails of the thumb and forefinger of his left hand to grow to an inch or more in length. With these "natural instruments" he could separate the eyelids and, at the same time, make gentle but firm pressure on the globe so that it was steadied and fixed, allowing him to make incisions and other motions with his right hand

Such illuminations as these had led me to inquire into the history of the instruments and other appliances invented to simplify cataract extraction with the development of surgical procedures which have done so much to allay the terrors which in former times seized the heart of the distressed subject at the prospect of so vital an operation

One may now ask what the Baron, at the end of the eighteenth century, had to say on how to avoid the "Inutility and Inconveniences of Specula," his "long experiences having taught him that these instruments are always unnecessary, that a dexterous person may easily seize a moment in which the eye is motionless" He stated his belief that "so

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<sup>1</sup> Wenzel, J. Treatise on the Cataract, translated from the French by J. Ware, London, C. Dilly, 1791, sec 12, p 78

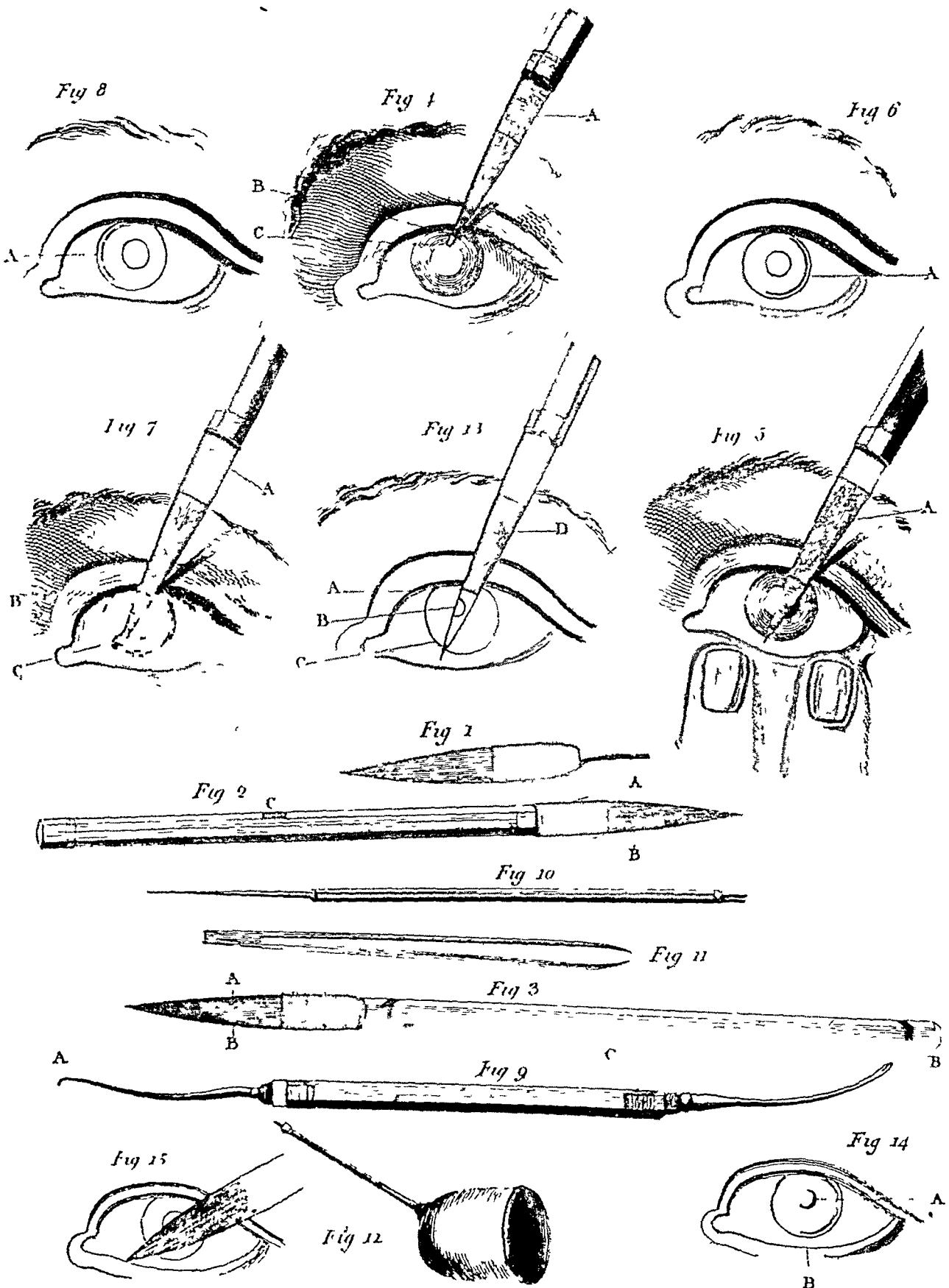


Fig 1—Above, drawings showing Wenzel's method of exposure and fixation of the globe, as well as incision with his special cataract knife, below Rumpelt's "silver thumble with its sharp attachment"

many different instruments not only render the operation more complicated but also are very liable to irritate and wound the eye," and, as he further declared, "they have been relinquished by the inventors themselves."

Wenzel could steady the globe while maintaining the perforation of the cornea with his cataract knife! He guardedly endorsed Rumpelt's "thimble with a sharp point attachment," devised by Fellen in 1782. This thimble was placed on the middle finger of the operator's left hand so as to impinge on the globe and in no way obstruct the use of his forefinger as it kept down the lower lid. Wenzel stated "that operators were often embarrassed by the wounding of the iris, that accident, [he felt] depended on the use of such instruments rather than on their being the means of preventing it."

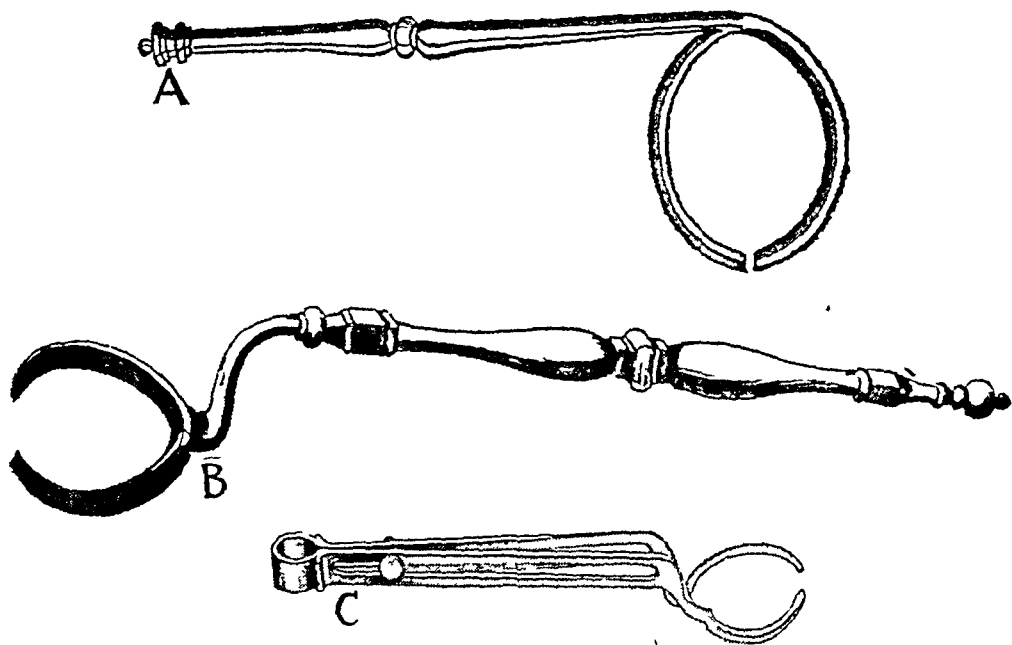


Fig 2—A, speculum devised by Pare (Pare, A. *Dix livres de la chirurgie, avec le magasin des instruments nécessaires à icelle*, Paris, J. le Royer, 1564) to dilate and hold the lids steady, it can be enlarged and reduced according to the size of the eye. B, ocular speculum to keep the eye open (Fabricius ab Aquapendente, H. *Opera chirurgica*, 1666). C, Cheselden's speculum, (Cheselden, W. *The Anatomy of the Human Body*, ed. 4, London, W. Bowyer, 1730).

Certainly, in those days, fingers were trained to perform dexterously many duties. The Wenzels, father and son, looked on speculums as inconvenient and complicating, rendering the operation intricate and stated that "in the hands of an unskilled operator by slight pressure [this instrument] would rupture the capsule of the vitreous humors", and the Baron could easily believe that the point of Rumpelt's instrument did "irritate and lacerate the membrane to which it was applied." In discussing the use of instruments, he insisted, that "the fewer instruments employed the less the eye is fatigued and, the more simple

the mode of performing the operation, the more certain will always be its success"

Waie, in commenting on Wenzel's disuse of instruments, and in the main agreeing with him, stated from his own extensive experience, especially in operations on congenital cataracts, that he had found it necessary to employ an elliptic ring with a handle attached with which by gentle pressure on the ring, he forced back the lids and fully exposed and steadied the globe

At this juncture it might be well to ask, "Which were the instruments the use of which Wenzel so strongly deprecated?" Had he seen the ellipsoid ring fixed rigidly in a rodlike handle, in use by Ambrose Pare in the middle of the sixteenth century? Or the cumbersome device of Fabricius ab Aquapendente, in the early 1600's? Or the somewhat similar one, more or less adjustable, devised by Cheselden in his busy career in the eighteenth century? All these required the constant attendant care of an assistant, all of them were likely to "render the operation more complicated, embarrassing the operator besides being more dreadful to the patient" The Baron refers to several other instruments in use in his days, but I must forbear from an enumeration of their inventors in this brief essay

A silk thread inserted through each side of the cornea, carried in a needle with the eye at its point, especially devised by M. Poyet,<sup>2</sup> he held to be useless for steadying the globe, because "that effect could be obtained by the cataract lancet" <sup>1</sup>

One may imagine some of the problems confronting the operator of those olden days. In attempting the incision, without some means of fixation, it was hardly possible for the surgeon to select the points of puncture and counterpuncture. The first contact of any sharp instrument was usually followed by jerking movements of the eyeball. The operator became impressed, inevitably, by the fact that the eyeball could not properly be steadied with the fingers. He was directed to wait until all muscular spasm had subsided before completing the section of the cornea. Fixation, with the lancet engaged, was especially dangerous because of the muscular contraction and general irritation from pressure on the globe. Many of the failures recorded were due to loss of vitreous through rupture of the hyaloid membrane. In time it became apparent that in order to expose the eyeball, instruments had to be invented with which to hold back the eyelids.

In the Museum of the College of Physicians, Philadelphia there is a great variety of long-forgotten instruments, many suggesting that fingers could not be excluded entirely, yet indicating that there are things that fingers cannot do. The most dexterous operator cannot sufficiently hold back the lid without exerting pressure on the ball.

<sup>2</sup> Poyet, cited by Wenzel, *J. Mem. Acad. de chir.* 2 253, 1753

## Operative cataract

### Sub IV

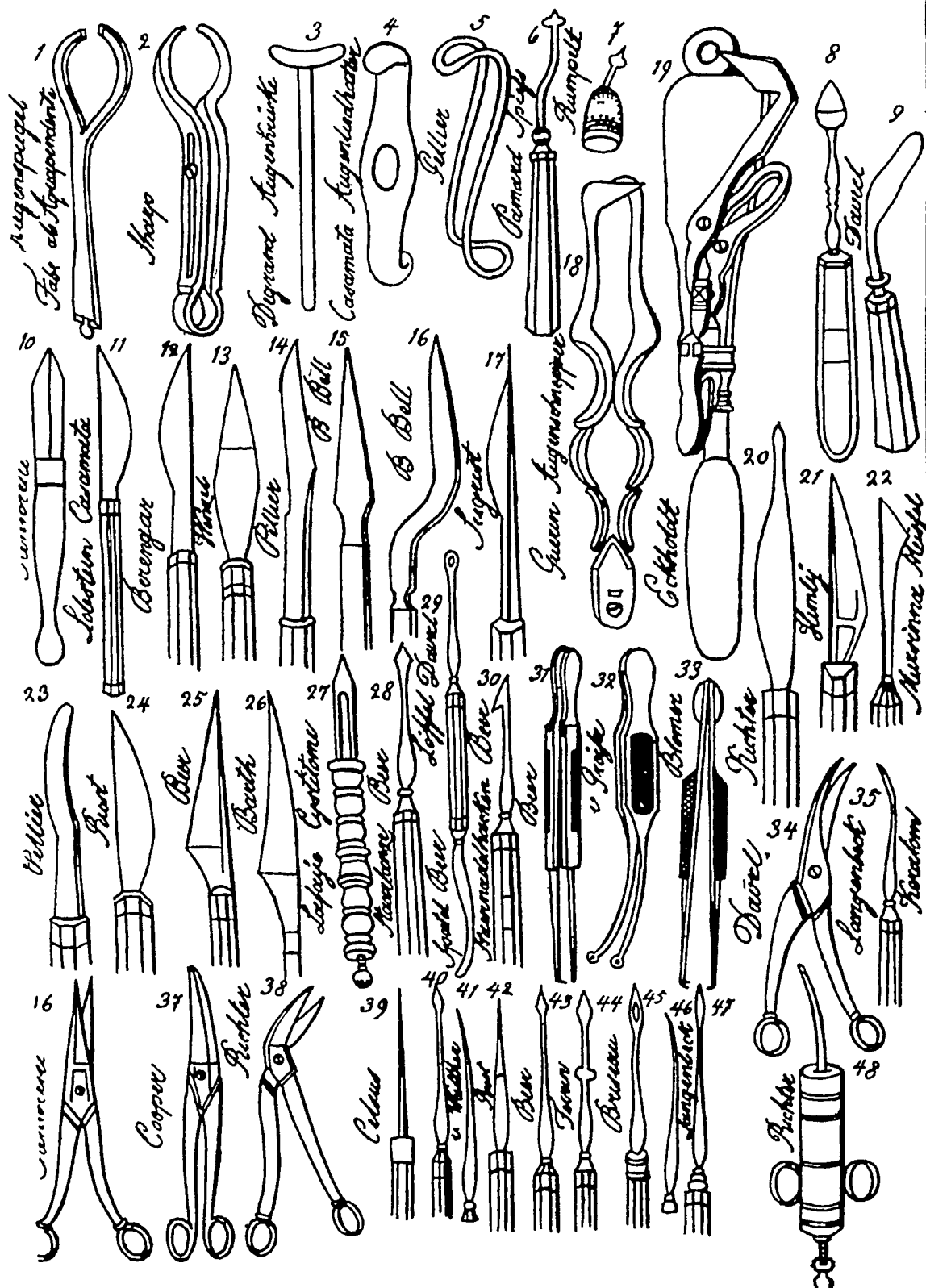


Fig 3—Instruments used in cataract operations (from Fritze, H E  
Miniatur-Armamentarium, Berlin, A Hirschwald, 1843)

It would seem that the Baron had not employed Pellier's "loop," devised about the middle of the eighteenth century, which consisted of a continuous thin silver wire with ends folded over, broad and hooklike,

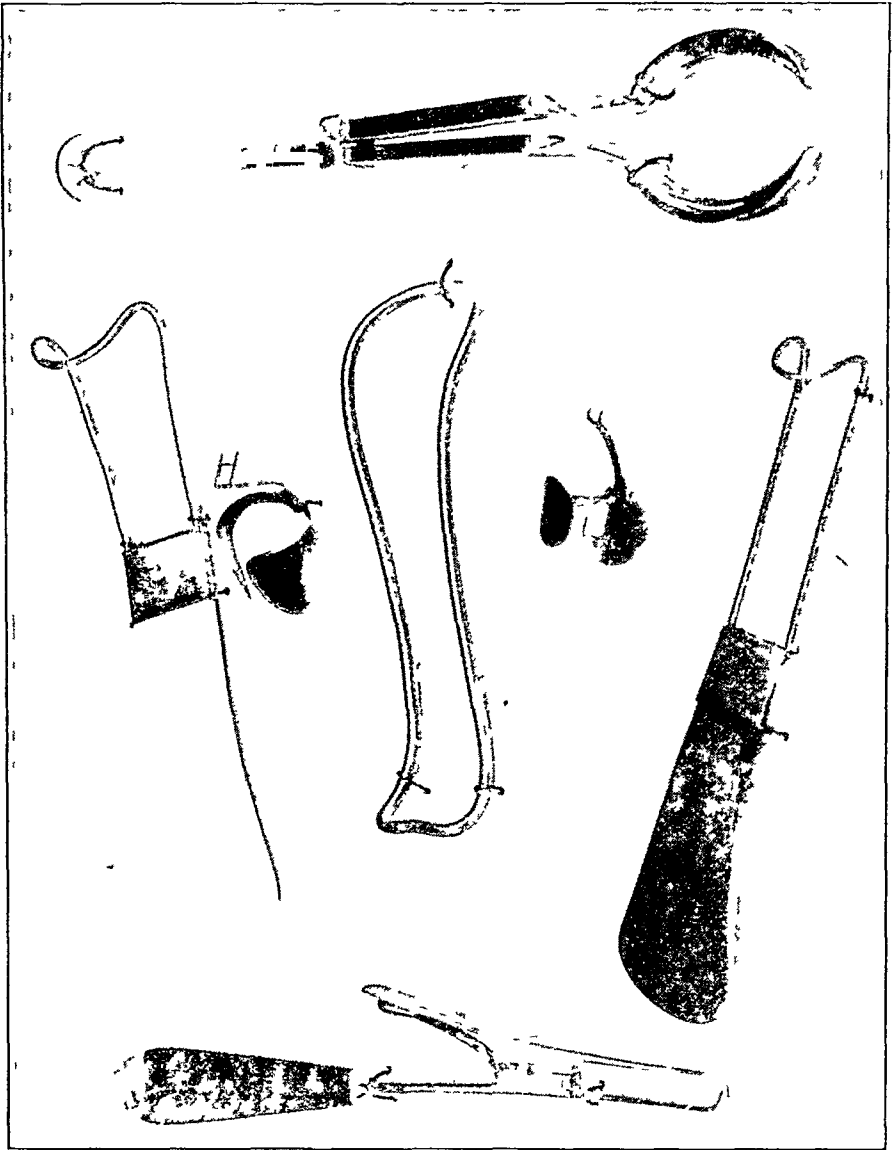


Fig 4—Display of antique instruments from the Museum of the College of Physicians, Philadelphia (by special permission), showing a Cheselden speculum, a Pellier lid elevator and two modifications, of later devising, of Rumpelt's *Fingerhut mit Stahlspieß* Forceps (about 1850), inventor unknown

for insertion under the upper lid, this served to withdraw the lid from the globe, the operator having only to manipulate the lower lid and steady the globe

In the early years of the nineteenth century, Saunders<sup>3</sup> the tounder of Moorfields, noted that he, in performing the operation on children, had adopted other methods of combating the "excessive mobility of the eye in the unsteadiness of the little patient" This he overcame by fixing the eyeball with Pellier's "elevator" (fig 5 *A*)

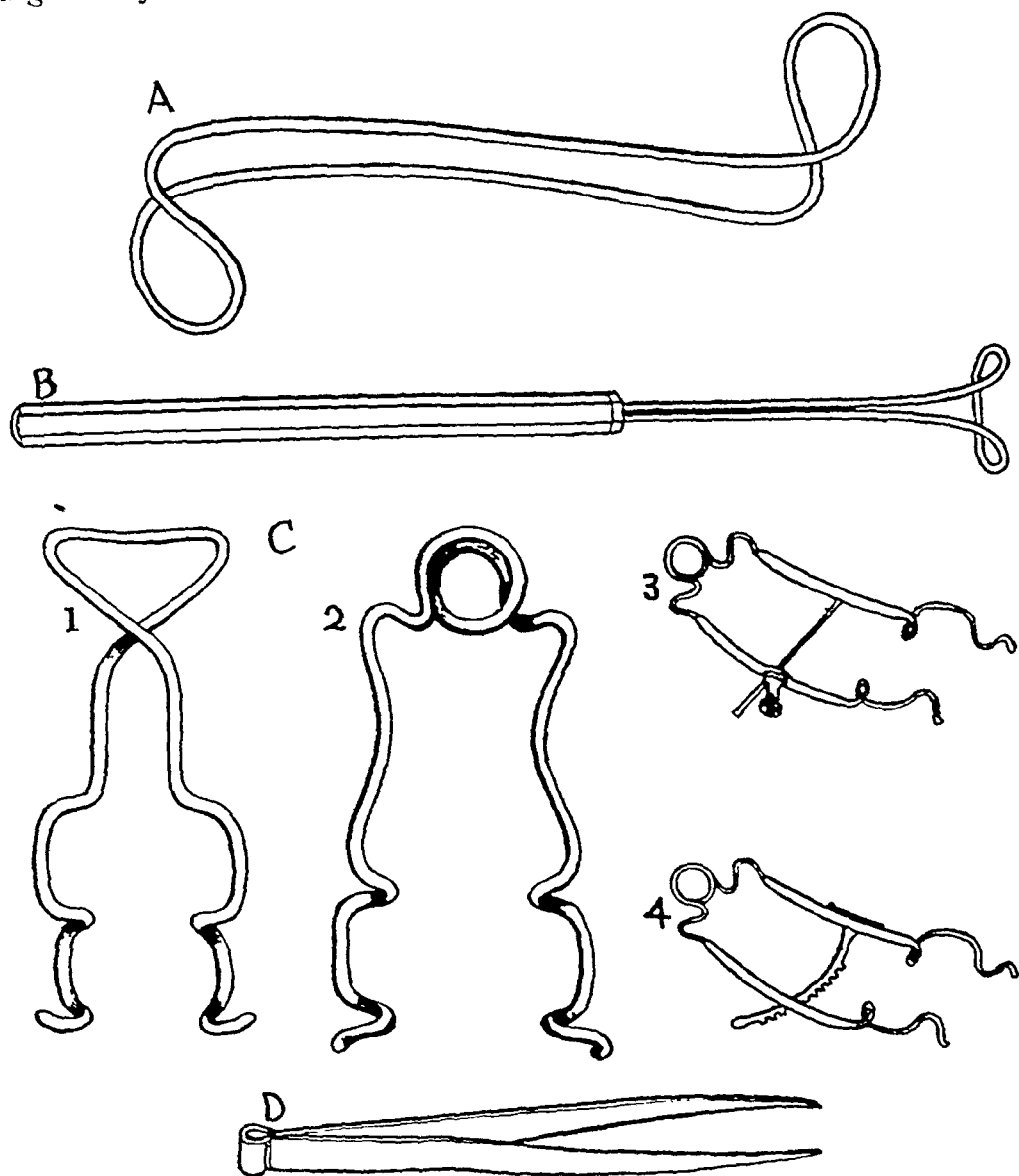


Fig 5—*A*, Pellier's eyelid elevator, *B*, Mackenzie's lid elevator (1854), *C*, early forms of speculums (1, Critchett, 1855, 2, Bitterich, 1858, 3, Bader, and, 4 Bowman, 1864), *D*, an eighteenth century forceps

[He] required four or five assistants to confine the patient. The first fixed his head with reversed hands, the second not only depressed the lower lid with his forefinger but also received the chin of the child as in a crutch. The third confined the upper extremities and body, the fourth—the lower extremities. The surgeon seated behind the patient took the Pellier elevator in one or the other hand, according to the eye, and the needle in the right or left."

<sup>3</sup> Saunders, J. C. A Treatise on Some Practical Points Relating to the Diseases of the Eye. London, Longman [and others], 1811, p. 117



The surgeon gently introduced the bore of the speculum under the upper eyelid, his assistant depressing the lower lid, and at the moment that he was about to pierce the cornea he "fixed the eye by resting the speculum with moderate pressure on the eyeball" Saunders emphasized that "by consent which can only exist between the hands of the same person, using the speculum merely as an elevator of the lid, he [the surgeon] can not only discontinue the pressure, [but] with facility renew or regulate the pressure at the moment in which it may be required"

As Mackenzie,<sup>4</sup> at the end of the first quarter of the nineteenth century, commented "the want of exposure on the part of the patient may in an instant defeat the most perfect dexterity of the operator" It should be of interest to read the details of his instructions to the two or more assistants as to the means of exposing the eye and maintaining its composure He himself steadied the eye by firm, yet the gentlest, pressure on the globe with his fingers There is no hint as to the use of an anesthetic "The fugitive eye is fixed without pressure by the fingers of an assistant and the operator To whatever side it turned it met with the point of a finger except towards the temple, where the knife is about to enter" Then, he declared, "Various sorts of specula, spikes and hooks have been invented for fixing the eye, but all of them, except the silver wire, commonly called Pellier's speculum, are now discarded" He occasionally employed it, especially in operations on children, for supporting the upper lid, either applying it to the outer surface or introducing it beneath the edge of the lid There was no better mode, however, of fixing the eye than by desiring the patient to look at the operator, who seized that moment for entering the instrument into the eye<sup>1</sup>

Such a "lid raiser" (fig 5 B) served Mackenzie until about 1850, when he modified it by fixing into an instrument handle a rod, the end of which was a loop bent like the Pellier hook This "elevator" was the prototype of the form now available in every instrument set

During the same period it became necessary to adopt a fixing instrument, to afford the operator a firm grasp of the globe without lacerating or perforating a fold of the conjunctival tissues At first the old form of dissecting forceps was employed, but that instrument was clumsy and ineffectual Von Graefe, with his accustomed technical and artistic inventiveness, overcame those defects by devising one of delicate limbs with teeth, two or more interlocking in the ends, which at once overcame the defects of the old forms Somewhat later, some one devised a wire spring speculum, the "bows" of which could be inserted under both the upper and the lower lid and which was so adjustable as

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<sup>4</sup> Mackenzie, W A Practical Treatise on Diseases of the Eye, London, Longman [and others], 1830

to be used without an assistant's aid George Critchett, about 1855, and Wharton Jones, a few years later, employed this principle in forms which they used, but they found that the pressure of the spring could not be relied on Bader and Bowman soon overcame this defect in pressure by affixing to the arms, spread to the desired width, a bar, secured with a screw or ratchet (fig 5 C)

Inevitably, it was forced on operators that an appliance should be devised with which to separate and hold back the eyelids It was deemed necessary that such an instrument should be self retaining, not likely to slip, stiff enough when in place to resist the action of a strong orbicularis muscle and capable of ready insertion and removal, it should exert no pressure on the globe, should be capable of adjustment to any desired width of opening and should never be in the way of an operator

In the collection at the College of Physicians, Philadelphia, are a modified Cheselden speculum, a primitive Pellier elevator and several modifications of it, as well as the modified Rumpelt thumb spike That spike was modified by Pamard, of Avignon, about 1840, by inserting it into an ordinary ivory handle The Pellier loop was modified by cutting one end free and inserting the arms of the remaining portion into an ivory, tonguelike handle, which might be used in plastic operations on the eyelids There are also several rather crude spring speculums

One may dwell for a moment on the story of how later discoveries solved the problem of the means of controlling the patient and the field of operation

Baron Wenzel did not deem it necessary to do much in the way of preparation prior to the operation He could rely on the steadfastness of the patients to control themselves and the reliability of his assistants in their cooperation with him When the sedative properties of the bromides and of chloral hydrate became known, these substances were given in fairly large doses in the preceding twenty-four hours Preparations of opium and morphine were administered sparingly

The discovery of the anesthetic powers of ether and chloroform proved a great boon to ophthalmic surgery No longer must the surgeon adopt a speedy technic, necessitated by the struggles and distress of the patient, not seldom to the great disadvantage of the latter Moreover, the employment of an anesthetic led promptly to modification of all operative procedures on the eye, as it had in general surgery In seeking to obviate the instability of the globe, surgeons found that such anesthetics not only quieted the patient but, by overcoming the tendency to contract the rectus and orbicular muscles, had the additional advantage of facilitating the exposure and fixation of the eyeball

Ophthalmic surgeons resisted employing chloroform for a long time on account of the vomiting which usually accompanied its use, they feared it might produce expulsion of the vitreous and hemorrhage within the globe. Furthermore, retching and vomiting hindered the operation, although the extraction might safely be completed after quiet was obtained. Moreover, there arose the question whether anesthetics should be used. The decision was determined by the courage of the patient! It was well known that many persons were capable of so great a degree of self control that the surgeon was enabled to perform the complete operation without an anesthetic!

When ether was first employed by the general surgeon, unpleasant effects were so frequent that Simpson suggested that chloroform might be substituted, and, in accordance with his dictum, it was used for many years. Yet chloroform occasionally caused death. The ophthalmic surgeon, therefore, hesitated to use the one or the other, and employment of an anesthetic became a serious matter on which he had to decide.

As already stated, anesthetics were rarely used in Europe, even as late as 1890, and surgeons, including some in America, avoided them except with nervous patients. Following the old custom of obtaining quiet and composure, the night before the operation they administered full doses of sodium bromide and chloral hydrate and repeated the doses an hour before operating. Morphine was sometimes given, yet opium was not always well borne. With children chloroform was used. Ether was employed for adults, yet for a speedy effect chloroform was given also.

In the late sixties and early seventies, as the administration of ether became more generally understood, it was found to be increasingly effective and safe, so that a steady return to its use was approved. In America, New England surgeons became increasingly adept in the administration of ether, and its quieting effects were seen to be sufficiently profound to favor the complete extraction of a cataract in a few brief minutes, their results influenced operators in England and on the Continent to use it.

Ether was employed by my distinguished teachers in most cases as late as the time of my own entrance into medicine. I assisted as the anesthetist many times, with satisfactory results, yet I was always directed "not to leave the hospital until assured the patients had fully recovered and their eyes were not uncomfortable." Dr. Norris repeatedly called attention to the fatal results he had known to follow the use of ether in patients with nephritis.

Many cumbersome and unwieldy contrivances were constructed with which to administer the fluid during the operation, none ever equaled a napkin, on which the ether was sparingly poured while the cloth was held over the face, by that simple means I have secured

complete relaxation and insensibility, in three or four minutes, having used less than 2 ounces (60 cc) of ether

Cocaine became of incalculable value because of its power to produce anesthesia by paralyzing the sensory nerves. Although this physiologic action had been generally known for years, it was not until 1884 that our own lately deceased fellow, Carl Koller, demonstrated in Vienna the practical value of cocaine in ophthalmic surgery. That discovery proved to be the final measure leading to surgical success and prevention



Fig 6—A, scene from Bartisch's "Augendienst", B, a medieval method of controlling the patient during operation for cataract (Bartisch, G. Augendienst, Leyden, 1522)

of the pain which operation had hitherto caused, in addition to its diminishing the great dread manifested by the sufferers. No longer were the surgeons' efforts frustrated by the constitutional effects produced by ether and chloroform anesthesia.

In times gone by, all the details of the cataract operation must have produced a formidable spectacle. Antique pictures tell one much. They show the patient fully dressed, as though he had just come in from the street and expected to return home. Or he might be seated in a chair,

his feet, legs, arms and hands lashed to the chair, his head held by an assistant, while the surgeon sat before him on a chair somewhat higher than the patient's. Years later, a number of assistants were usually employed. To take the place of an assistant, Laurence, in England, constructed a head clamp to be affixed to the operative bed. About 1850, the patient reclined or lay in bed, if not on a table, or, as there used to be at the Wills Hospital, a lounge! The patient walked into and



Fig 7—Photograph by Himly and Ruete, from Saemisch, T. Handbuch der gesamten Augenheilkunde, Leipzig, W. Engelmann, 1911, vol 14, p 2

departed from the operation room in that revered hospital, and as late as 1912 I witnessed such an incident at a famous institution in Europe.

In conclusion, let me describe two scenes, in striking contrast to each other. The first is a detail from Joseph Warner's account, as detailed by Chandler.<sup>5</sup> Warner, a contemporary of Wenzel, was surgeon at Guy's Hospital.

<sup>5</sup> Chandler, G. Treatise on Diseases of the Eye, and Their Remedies, London, T. Cadell, 1780.

An assistant stands behind the patient, who puts his right hand under the patient's chin, after having covered the right eye, supposing it to be the left which is to be operated upon, the assistant then places the back part of the patient's head on his breast, at the same time directing the face upwards, to prevent the sudden discharge of the vitreous humor. He afterwards lifts up the superior eyelid with two or more of his fingers, taking care not to press upon the globe of the eye above, the operator at the same time depresses the inferior eyelid, with this precaution, not to press upon the inferior part of the globe of the eye till the incision is made. The patient must look straightforwards, and a little upwards. The operator now fixes his right elbow upon his right knee, after having put his right foot firmly on the patient's seat for this purpose. He then suddenly and resolutely introduces the point of his knife through the external part of the cornea.<sup>5</sup>

Today, a patient, having been admitted to the hospital after all studies have been made as to his general condition of health, and with the eye and adnexa free of possible infectious matter, is quieted with barbital and other sedatives and is placed in bed during the twenty-four hours prior to his entrance into the operation room. Then, after administration of cocaine or similar local anesthetic, perhaps by injection into the orbit, the speculum is adjusted, with exposure of the globe, which is then seized with delicate forceps and steadied so that the incision can be made and the extraction pursued—all without pain or discomfort. The patient may perhaps ask at the termination of the procedure when the surgeon will begin the operation, so that he might aid him in every way possible.

No longer could the Baron have declared that "pain attending cataract extraction is unavoidable," if, recently, he could have stood at the bedside with my house surgeon, to whom was given the care of an exceedingly timorous aged lady. No longer might he have dwelt on "the great difficulty under which the operator who employs instruments for the fixing of the eye labors from the want of a free, unconfined and unembarrassed use of both hands."

317 South Fifteenth Street

## Obituaries

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### GRADY EDWARD CLAY, M D 1889-1946

Grady Edward Clay, only child of Augustus C Clay and Elizabeth Chupp, was born Aug 12, 1889, in the village of Walnut Grove, Walton County, Ga. During his last illness he retired to the plantation where had lived five successive generations of his family, and died on July 11, 1946.

Dr Clay obtained his primary education in the county schools and, at nearby Oxford, Ga., he graduated in 1910 from Emory College. He received his medical degree from the University of Michigan in 1914, and for the next three years he was resident physician in the department of ophthalmology, under the tutelage of Dr Walter R Parker. He returned to Georgia in 1917 to practice his specialty in Atlanta but soon entered the Army in World War I. After serving as ophthalmologist in a base hospital in France, he was discharged in 1919 with the rank of captain.

On resumption of his practice, Dr Clay became associated with the department of ophthalmology of the Emory University School of Medicine. His ability and interest in teaching attracted notice, and his promotions were rapid. In 1939 he was made chief of the department of ophthalmology and in 1943 full professor. With the financial aid given the department in recent years by his influential friends and patients, special facilities for teaching and investigation became available, and a laboratory for ocular pathology and bacteriology was established.

In his lectures to the undergraduate students Dr Clay was positive and straightforward, which characteristics made him an excellent teacher. Most instructive, to students and staff alike, were his ophthalmoscopy rounds of patients in the medical and obstetric wards of the city hospital. His great interest in medical ophthalmology, especially the vascular changes in the retina, was reflected in the widespread use of the ophthalmoscope by the students and by the members of the departments of obstetrics and of internal medicine.

Dr Clay was an indefatigable worker, and because of his large private practice his hours were long. His private hospital work was done at Emory University Hospital, and there, through his efforts, many reforms were established for the more efficient handling of patients with ocular disease. In this hospital on Tuesday afternoons, he held

his operative clinics, which were always varied and were frequently attended by visitors. He was an advocate of the round pupil intracapsular extraction of cataract, and his technic and skill were superlative.

Dr. Clay's contributions to ophthalmologic literature were not numerous, but an analysis of his major articles will show originality, careful preparation and a wide experience of the subject. He wrote especially



GRADY EDWARD CLAY, M.D.

1889-1946

on the subject of angioid streaks, and his number of personally collected cases was almost 70. He also contributed much to the knowledge and understanding of the changes in the retinal vessels associated with cardiovascular-renal disease. The subject had fascinated him for



twenty-five years, and to the last he worked to have established a more uniform and simple classification of these changes

The untiring devotion of Dr Clay to the welfare of his patients, his constant efforts to provide more effective ophthalmologic service and treatment, his ready application of newer and better methods, were all representative of his dogged, ever searching spirit, which never ceased fighting when confronted with a desperate case

Perhaps the greatest contributions that Dr Clay made to medicine and to society were his interest in the welfare of the poor and underprivileged and his love and understanding of the country folk, manifested not only in free clinics at Grady Hospital and Emory University Hospital but also at his farm home, where on Sunday afternoons he would often see the poor of his neighborhood, providing any necessary hospitalization at his own expense

Dr Clay possessed a magnificent physique and a commanding appearance. He was a forceful and enthusiastic speaker and was a frequent and popular guest at many postgraduate and society meetings. His cordiality, friendliness and winsome smile attracted people.

Dr Clay loved sports and outdoor life. His favorite pastimes were hunting and fishing, but his obsession and hobby was his nearby farm where he took great pride in his herd of registered Hereford cattle.

In 1915 Dr Clay married Miss Eleanor Hall Solomon, of Macon, Ga. Two children, Grady Clay Jr., of Louisville, Ky., and Mrs. Eleanor Clay Calhoun of Atlanta, Ga., and 3 grandchildren survive.

Dr Clay was vice chairman of the Section of Ophthalmology of the American Medical Association and was a former member of the American Board of Ophthalmology. He was a member of the Methodist faith and a liberal contributor to his country church. His college fraternity was Phi Delta Theta, and he held membership in the national scholastic societies of Phi Rho Sigma, Sigma Xi, Phi Beta Kappa and Omicron Delta Kappa.

We who had worked daily by the side of Dr Clay for nearly thirty years knew his worth as a physician, humanitarian, teacher and friend. Taken in the prime of life, with many useful years before him, his loss is tremendous. To his legion of friends, a hero has fallen!

"He was a man, take him for all and all,  
I shall not look upon his like again"

F PHINIZY CALHOUN, M D

# Abstracts from Current Literature

EDITED BY DR WILLIAM ZENTMAYER

## Conjunctiva

CHOICE OF SULPHONAMIDE IN THE TREATMENT OF OPHTHALMIA NEONATORUM ARNOLD SORSBY and E E HOFFA, Brit J Ophth. 29: 141 (March) 1945

On the basis of 333 cases of ophthalmia neonatorum treated with a standard dose of five sulfonamide compounds, it is concluded that the least tolerated drug is sulfanilamide and that sulfapyridine is less well tolerated than sulfamezathine, sulfathiazole or sulfadiazine

In their efficacy against the infection, as distinct from their tolerance by the babies, these five substances are not strikingly different

With the standard dose employed in this series, some 30 to 40 per cent of infants show clinical cure within three days Well over 80 per cent of the total are cured by the end of eight days' treatment

Gonococcic ophthalmia neonatorum responds more readily than other varieties of ophthalmia Cases showing inclusion bodies respond satisfactorily An initial severity does not affect the course unfavorably Many severe cases clear rapidly Irrespective of the causal organism, some 15 per cent of cases show a sluggish or poor response The routine management of cases is described

W ZENTMAYER.

THE SOCIAL AND MEDICAL PROBLEMS OF PHLYCTENULAR DISEASE IN DUBLIN J B McAREVEY, Irish J M Sc, July 1944, p 201.

The object of the inquiry was to determine the trend of phlyctenular disease in Dublin, the age and sex incidence, the seasonal incidence, the types of the disease and the occupation of parents of children suffering from the disease The information was obtained from an analysis of 2,470 new cases at the Royal Victoria Eye and Ear Hospital, Dublin The periods selected represent World War I, the present war and a normal period immediately before the present war The study warrants the conclusion that basically phlyctenular disease is a manifestation of malnutrition It is a disease of the poorer classes, in whose diet the essential proteins necessary to growth and normal development are practically absent, the only source of these substances available to most of the children being milk, in limited quantities; as a result, they suffer from a low grade malnutritional anemia, with a deficiency of some essential vitamins

It is interesting to note that the evidence of tuberculous infection was positive 1 The reaction to the tuberculin test was positive in 85.9 per cent of children (13 per cent of controls) 2 Roentgenograms of the chest showed positive evidence in 37.3 per cent of children (20 per cent of controls) 3 There was a history of contact in 5.5 per cent (and of possible contact in 2.9 per cent) 4 The incidence of sanatorium care was 11.8 per cent The nature of the tissue reaction points to an allergic response

W ZENTMAYER

### Congenital Anomalies

BILATERAL PARTIAL ECTASIA OF THE NERVE HEAD WITH PERIPAPILLARY ECTASIA I S MACGREGOR, Brit J Ophth 28. 618 (Dec) 1944

The case described is one of partial ectasia of both optic disks with complete peripapillary ectasia. The disks were not completely excavated. The picture is remarkably similar to the late results of traumatic avulsion of the optic nerve with preservation of the continuity of the vessels except that glial proliferation at the nerve head is usually pronounced in cases of proved avulsion. The condition is regarded as a congenital anomaly of the optic disk. It may be a rare form of birth injury resulting in partial avulsion of the optic nerve rather than a developmental failure at the disk.

The article is illustrated

W ZENTMAYER

CONGENITAL DEFECTS AND RUBELLA Brit M J 1 635 (May 5) 1945

In Australia 109 cases of congenital defects associated with maternal rubella have been reported. Reese, Erickson and Simpson report 16 additional cases in other countries. "The main points of agreement in the published data appear to be (a) that the association is with rubella and not with other transmissible diseases (though not without exception), (b) that the risk of congenital defect is greatest if the rubella occurs in early pregnancy (i.e., within the first three months) and (c) that there are infants with congenital defects in which no link with a maternal transmissible disease can be traced. The general inference is that the unknown virus of rubella (with virulence possibly enhanced in the war years) is showing the preference of certain viruses for developing embryonic tissue. This it does by attacking the foetus via the placental circulation just at a time when important developmental changes are taking place in the foetal heart and eye. The high incidence of congenital heart disease suggests to these observers that the rubella virus has a primary affinity for vascular tissue, the lens damage being explained by possible indirect action through the hyaloid artery."

The author asks whether the association between presumed rubella and congenital defects is a significant one or whether it arises from pure chance. The question also arises: Was the maternal disease rubella? According to the author, in some cases the diagnosis was in retrospect unsatisfactory and in others hardly justifiable. He believes that the possibility of a chance association between congenital defects and true maternal rubella cannot be excluded and suggests that a systematic investigation of rubella in pregnant women be instituted.

ARNOLD KNAPP

### Cornea and Sclera

A FREQUENT AND DEFINED TYPE OF KERATITIS E ROMERO, Arch Soc de oftal hispano-am 3 458 (Nov-Dec) 1943

The author describes a condition of the cornea produced by alcohol vapors, entirely different from the burn produced by direct action of

the liquid. The lesion produced is a superficial, faint central erosion of the epithelium, with no opacity. It takes the stain poorly but can be detected by the ridge formed around it by the peripheral zone of normal epithelium. The patient with such a lesion comes to the oculist complaining of pain, sensation of a foreign body, photophobia, blepharospasm, congestion and lacrimation, without pathologic antecedents, a history of injury from a foreign body or any apparent corneal lesion. There is a history of exposure to alcohol.

H F CARRASQUILLO

PHLYCTENULAR KERATOCONJUNCTIVITIS OBSERVED IN THE GAFFNEY AND GUINLE OUTPATIENT DEPARTMENT IN SANTOS D LIVRAMENTO PRADO, Arq brasil de oftal 5: 51 (April) 1942

Four hundred and eight patients with phlyctenular keratoconjunctivitis were observed in the outpatient department of this institution. 202 children were boys and 180 girls, and 26 patients were adults. The etiologic factors are discussed.

In 1936 the author performed Piquet's cutaneous test in 36 cases of lymphatic keratoconjunctivitis and obtained a positive reaction in 100 per cent. A roentgenogram of the lungs was taken in 14 cases, the results being as follows. In 52 per cent of the 14 cases there were incipient pulmonary disturbances, the lungs being normal in the remaining 48 per cent.

Therapy consisted in injections of Gaduzan, 2 cc, calcium gluconate in a 10 per cent solution, tuberculin, and the usual ocular treatment with such means as strong protein silver, Noviform (a bismuth preparation) and vapor baths.

Progressive improvement was noted, and a cure was effected within twenty to thirty days. In 6 of the cases in which no pulmonary alterations were noted rigorous treatment with preparations of vitamins C and B was instituted, cure being effected in twelve days.

This seems to show that lymphatic keratoconjunctivitis may be due to an avitaminosis, although the possibility of a tuberculous causation seems to be definitely established.

M E ALVARO

### Experimental Pathology

EXPERIMENTAL PHOTO-RETINITIS J C ECCLES and A J FLYNN, M J Australia 1: 339 (April 15) 1944

The authors, carrying further the investigations of Verhoeff, Bell and Walker (Pathological Effects of Radiant Energy on the Eye, *Proc Am Acad Arts & Sciences* 51: 630, 1916) exposed the retina of anesthetized rabbits to direct rays of the sun, admitted through a round hole in a metal plate fixed close to the pupil. Lesions obtained at first were very small, and to enlarge them one tube of a Zeiss binocular was used as a telescope. A formula was devised to calculate the calories per square centimeter per minute at the site of the retinal image, and exposures were carried out with and without absorption filters. The eyes were examined ophthalmoscopically and, later, microscopically.

It was found that with thirty seconds' exposure lesions were produced when the radiation was above 50 calories per square centimeter per minute but not when the radiation was below 40 calories. Ultra-violet rays were absorbed and did not reach the retina. Microscopic examination revealed an amount of destruction of cells proportionate to the radiation.

The authors found that radiation of an intensity as high as 100 calories per square centimeter per minute requires several seconds to produce lesions, and they conclude that rapid glances at the sun are therefore innocuous. They also point out that protective glasses with high absorptive powers for visible rays may be dangerous when used for viewing the sun if they transmit infra-red rays.

G M BRUCE

### General Diseases

TUBERCULIN SENSITIVITY AND OCULAR PROCESSES M F VIGNOLI  
and C GARBINO, Arch de oftal de Buenos Aires 18 713  
(Dec) 1943

The study of the index of tuberculous infection carried on extensively in various countries in the past several years has altered the belief that this infection occurs only in very early life. In Montevideo the maximum incidence of infection is reached at the age of 30 years. Fifty per cent of the school children give a negative reaction to tuberculin in a dilution of 1:10 in the Mantoux test.

In Argentina, of 37,139 conscripts, 41 per cent gave a negative reaction. In Buenos Aires, in 1940, according to the studies of Raimondi and associates, 40 per cent of the youth from 14 to 20 years of age were found free from infection. It is therefore established that the tuberculin allergy may help in the diagnosis of tuberculous ocular conditions not only in children but in adults.

To establish a state of allergy, a negative response to the Mantoux intradermal test, to first and second concentrations of purified protein derivative or to a 1:10 dilution of Koch's old tuberculin is necessary. A maculopapule larger than 10 mm is considered a positive reaction. If smaller, the reaction is considered doubtful. If the primary infection is of recent occurrence, the reaction may be negative, and tests must be repeated thirty or sixty days later.

Studies were made on 75 patients. The threshold of allergy was determined, and roentgenographic studies of the chest were made on these patients. New determinations of the threshold were made at various intervals, and a graphic curve of the sensitivity to tuberculin was traced.

The authors give in detail the technic used in their tests and list the results obtained on the 75 patients studied, including 19 ocular conditions which might have a tuberculous origin. Of the patients, 27 were men and 48 women. The ages ranged from 10 months to 52 years, and the majority were between 15 and 30 years of age.

The number of anergic subjects was 9, or 10.2 per cent. Of the allergic patients, 91.6 per cent were tested for hyperergy, and 72.7 per cent gave positive reactions to dilutions above 1:1,000,000.

In cases of phlyctenular keratoconjunctivitis the threshold ranged from a positive reaction to a dilution of 1:10,000,000,000 and a negative

reaction to a dilution of 1 : 10. For 25, out of a total of 35 patients, the threshold concentration was above 1 : 1,000,000.

The existence of hypersensitivity to tuberculin in the presence of a pathologic process in the eye is not positive proof of a bacillary origin but is information to be added to the clinical examination. However, when the threshold is determined in the way advocated by the authors and some correlation is shown between the sensitivity and the lesion, the one being increased with aggravation of the other or diminished when the process improves, the disease in all probability is tuberculosis. In contrast to the cases of intense hyperergy, when the reaction is negative to concentrations of 1 to 10, tuberculosis may be excluded. If the case is one of hypoergy the diagnosis of tuberculosis is in doubt.

H. F. CARRASQUILLO

### Hygiene, Sociology, Education and History

THE ANTIQUITY OF OPHTHALMOLOGY. W. B. INGLIS POLLOCK, Brit J Ophth 29:252 (May) 1945

This interesting historical article does not lend itself to abstraction. In brief, as stated by the author, it has been shown that ophthalmology was in existence in Egypt during the days of the Old Kingdom, before 3,000 B. C., and also in Mesopotamia between 2000 and 1500 B. C. It was the first specialty to be set up, by reason of the serious results of the various, extremely frequent, diseases of the eye which oculists were required to treat, and was an effort then, as now, to prevent them from the dire results of failure.

W. ZENTMAYER

INDUSTRIAL OCULAR LESIONS AS COVERED BY THE ARGENTINE LAW. JOSÉ A. SENÁ, Arq brasil de oftal 7:213 (Dec) 1944

A historical summary of the legislation for industrial accidents to the eyes is presented. Various statistics on industrial ocular accidents in Argentina and in the United States are given, those of Argentina being presented in greater detail. The occupational diseases, defined in chapter 11, article 145, of the Argentine law as being "those due exclusively to the work undertaken by the patient in the exercise of his occupation," are discussed. These diseases are divided into three groups: (1) purely local disorders which may have much to do with industrial accidents—the external ocular diseases, (2) ocular lesions resulting from poisoning or a general infectious condition which may be imputed to work, and (3) visual disturbances resulting from bodily fatigue. In the last group miners' nystagmus and visual alterations due to prolonged eyestrain in certain occupations are included. The following subjects are considered in detail: external ocular diseases, the eye and occupational poisoning, trachoma, ocular tumors, ocular syphilis, ocular tuberculosis, exophthalmic goiter and retinal detachment in relation to industrial accidents, ocular traumas and their general repercussion, and ocular traumatic neuroses and psychoses. The author comments on the Argentine laws relating to industrial accidents.

M. E. ALVARO

## Injuries

PENETRATING INJURIES OF THE EYE W F MONCREIFF and K J SCHERIBEL, *Am J Ophth* 28 1212 (Nov) 1945

This is a statistical study Two practical conclusions are drawn, namely, that 20 per cent of penetrating injuries could be eliminated, or at least minimized, by eliminating glass from the domestic economy and that in a smaller percentage prompt enucleation should be done

W S REESE

NON-MAGNETIC INTRAOCULAR FOREIGN BODIES Editorial, *Brit M J* 1 228 (Feb 17) 1945

Aluminium is being used increasingly in the manufacture of projectiles, and except for shell and bomb fragments most missiles may now be regarded as nonmagnetic This was described by Savin in a Hunterian Lecture two years ago, and this author has now brought the subject up to date in a paper recently read before the Royal Society of Medicine The proportion of magnetic and nonmagnetic foreign bodies in the eye is 1 6, and this is still more unfavorable in air raid casualties, in which the proportion is 1 9 The attending infections were favorably influenced by the use of sulfonamide compounds, but the problem of these retained foreign bodies is increased by ignorance of the reaction of the eye to aluminium

Savin has made a number of experiments to study the reaction of the eye to aluminium He finds that pure aluminium may be completely absorbed but more often the fragment becomes coated with a white deposit of aluminium hydroxide or with fibrin and gelatinous material Changes in the lens and vitreous were late results in almost all cases, and there was evidence of retinal damage It is clear that aluminium is not inert and that its removal from the eye is difficult It is essential that an accurate localization of these nonmagnetic foreign bodies be made, and a successful forceps extraction is more likely in the anterior segment of the eye than in the posterior segment Savin concludes that until there is an improvement in technic the removal of these bodies should only be attempted in cases in which clinical observations show the foreign body to be deleterious

ARNOLD KNAPP

## Lacrimal Apparatus

DACRYOCYSTORHINOSTOMY THE DUPUY DUTEMPS-BOURGUET-VALLE PROCEDURE E J J LAGOS, *Arch de oftal de Buenos Aires* 18 639 (Nov) 1943

The author gives an account of his experience with the classic technic In his opinion, Valle has simplified the procedure with the instruments he has designed, the time of operation being shortened and less instruments being needed than with any other method

Lagos advocates the operation of dacryocystorhinostomy instead of extirpation of the lacrimal sac, the latter to be done in cases of new growths, tuberculosis or too small a sac Previous conservative treat-

ment with probing and irrigations is recommended. Intranasal examination before the operation is important.

The author has performed the operation in more than 100 cases, with gratifying results. In only 3 cases did profuse intranasal hemorrhage occur, and in 1 case there was slight suppuration. A detailed description is given of the technic of the operation, some of the Dupuy Dutemps instruments and those designed by Valle being employed. The osteotome is preferred to the burr or the chisel and hammer, being less liable to injure the nasal mucous membrane.

The indications and contraindications to the operation are given.

H F CARRASQUILLO

### Lids

TOTAL RECONSTRUCTION OF THE UPPER LID (BLEPHAROPOIESIS).

W L HUGHES, *Am J Ophth* 28:980 (Sept) 1945

Hughes comments on the importance of the upper lid in protecting the globe and discusses the reconstruction of the lid. He reports a case and describes all the stages of repair, using numerous illustrations.

W S REESE

MER BROMIN [MERCUROCHROME] IN TREATMENT OF BLEPHARITIS

J DE P XAVIER, *Arq brasil de oftal* 7:232 (Dec) 1944

Owing to the difficulty of obtaining the Pyoktanin (gentian violet medicinal) drugs in pencil form, the author requested a chemist to make up a merbrom (mercurochrome) pencil, consisting of pure acacia, distilled water and approximately 80 per cent of merbromin. This was used in 10 cases of ulcerative blepharitis, 9 cases of crustal blepharitis and 8 cases of squamous blepharitis. Daily applications were made and satisfactory results obtained. Squamous blepharitis was cured after ten to fifteen treatments, the more serious forms (ulcerative blepharitis) requiring further applications in order to obtain the same results. A bibliography is included.

M E ALVARO

### Neurology

OCULAR NEUROVEGETATIVE SYSTEM IN RELATION TO OCULAR TENSION AND PREGNANCY. F VIDAL and S A DURANDO, *Arch de oftal de Buenos Aires* 19:32 (Jan) 1944

The hypothalamus controls the visceral functions by two different mechanisms. The lateral part of the organ is the chief regulating center of the sympatheticoadrenal system, and the medial part, of the parasympatheticohypophysial system. Ocular tension is physiologically controlled by these two systems, being increased by the first and decreased by the second. During normal pregnancy the parasympatheticohypophysial system is more active, and so the ocular tension during this period stays at the lower normal levels, or even below.

One hundred normal pregnant women between the ages of 15 and 40 were examined. The Schiötz and MacLean tonometers were used.



The measurements ranged from 15 mm Schiøtz and 22 mm MacLean, in 56 per cent of patients, to 11 mm Schiøtz and 14 mm MacLean, in 7 per cent

H F CARRASQUILLO

THE CENTRAL SCOTOMA AS AN EARLY SYMPTOM IN THE DIAGNOSIS OF INTRACRANIAL CONDITIONS A GARCIA MIRANDA, Arch Soc oftal hispano-am 4. 30 (July-Aug) 1944

Central scotoma is a frequent symptom which is not properly evaluated. It is usually taken as a sign of retrobulbar neuritis, without regard to the fact that it may be an early indication of an intracranial condition then amenable to treatment.

In cases of tumor of the frontal lobe, hypophysial neoplasm, arteriosclerotic changes in/or aneurysm of the internal carotid artery, optochiasmatic arachnoiditis and meningioma of the lamina cribrosa of the ethmoid bone, a central scotoma may occur early in the course of the disease.

H F CARRASQUILLO

MOTOR-SENSORY OPHTHALMOPLÉGIA W DUQUE ESTRADA, Rev brasil de oftal 2 135 (March) 1944

Estrada discusses the neuropathologic syndromes caused by lesions of the motor and sensory nerves in their orbital course. He divides them into (1) syndrome of the sphenoid fissure, either with or without amaurosis, (2) syndrome of the petrous-sphenoid junction (Maurice-Jacod), and (3) syndrome of the external wall of the cavernous sinus (Foix).

The author reports the case of a man with a syndrome of the sphenoid fissure. He interprets the significance of the motor, sensory and visual disorders as well as the presence of exophthalmos for the diagnosis of a lesion of the nasal nerve due to a tumor of the sphenoid fissure. In the case he reports the laboratory, roentgenographic, otorhinolaryngologic and early clinical examinations did not aid in diagnosis. Roentgen therapy failed. A clinical diagnosis of blastoma of the sphenoid fissure, made late in the course of the disease, was verified at necropsy.

W ZENTMAYER

### Operations

RECONSTRUCTION OF THE LIDS W L HUGHES, Am J Ophth 28 1203 (Nov) 1945

Hughes discusses surgical reconstruction of the lids. He concludes that normal structures of the lid should be used as replacement tissue or, if such tissue is not obtainable, tissue as similar to the original as possible. A second choice is (a) for the skin of the lid, full thickness skin from the cephaloauricular angle, to be used as a free graft, or a pedicle graft, (b) for the conjunctiva, mucous membrane from the mouth or thin split skin, and (c) for the tarsus, cartilage from the ear or rib.

W S REESE

USE OF APONEUROSIS OF GASTROCNEMIUS MUSCLE FOR PLASTIC  
OPERATIONS ON THE CONJUNCTIVA FORNIX G BURSUK, Vestnik  
oftal 23:13, 1944

This paper is a preliminary report

Bursuk used the aponeurosis of gastrocnemius muscle for plastic operations on the conjunctiva fornix, in 2 cases for partial and in 3 cases for complete restoration of the conjunctival sac This material was found to be adequate, as it is firm, does not shrink and is plastic enough to take a given shape and often complete union with the conjunctiva takes place The color of the transplant changed in one and a half to two weeks and took on the color of the conjunctiva

A prosthesis was usually put in the day after the operation, so that the transplant could take the shape of the prosthesis The flap was taken from the middle third of the muscle, the shape of the incision was semielliptic (for prevention of opening of the sutures), with the base below and lateral to the tibial crest

The results are reported in case histories

O SITCHEVSKA

Orbit, Eyeball and Accessory Sinuses

A NEW METHOD AND APPLIANCE FOR GRAFTING EYE SOCKETS  
H P PICKERILL, Brit M J 1:596 (April 28) 1945

To avoid the great difficulty in getting a glass eye to fit the socket one has made, the author has reversed the process and makes the socket fit stock-sized glass eyes A stock-sized glass eye is first obtained, this is enlarged with wax and duplicated in acrylic resin by taking molds in stent, plaster or gelatin Two holes are drilled through this mold, of the same size as the nozzle of a Record syringe One hole is drilled exactly in the center of the pupil Into this hole is fitted a pin about  $1\frac{1}{2}$  inches (38 cm) long, with a little shoulder, which prevents it from going too far in After the socket has been prepared in the usual manner a one-half thickness of skin graft is cut with the dermatome, fixed on the acrylic mold and inserted into the socket The pin is inserted and fixed with strips of strapping from forehead to cheek and nose, so that the pin, which is exactly in the place of the future pupil, will be in the correct position The lids are then sutured After ten days some discharge appears The pin is removed, and the socket is gently irrigated through the holes provided in the socket The pin and strapping are then replaced The appliance is left in position for one month, it is then removed every other day for cleaning and is reinserted, pressure being kept up by elastoplast strips In not less than two months the appliance can be discarded, and the stock glass eye will be found to fit perfectly

There is no coordinated movement, in a grafted eye, movement has never been possible The method gets over the almost insuperable difficulty of having a special eye made for every grafted socket

ARNOLD KNAPP

### Refraction and Accommodation

CATMIN LENSES S KAMELLIN, *Am J Ophth* 28 993 (Sept) 1945

Kamellin describes the catmin lens as an image-minifying lens, of special value in certain cases of unilateral aphakia. He reports 10 cases from the files of the late Dr S R Gifford.

The advantage of catmin lenses lies in the fact that they are reversed telescopic lenses which are of value in certain cases of unilateral aphakia in children and in adults in which contact lenses cannot be used to maintain binocular vision. The disadvantages of catmin lenses are that cosmetically their appearance leaves much to be desired and the field of vision with their use is restricted about 23 per cent.

The author reaches the following conclusions. Catmin lenses are of benefit in many cases for the maintenance of binocular vision and may be added to the armamentarium of the ophthalmologist, to be used in cases in which the patient does not object to the appearance of the lens and does not object to the restriction in the field of vision and in which contact lenses cannot be prescribed.

W ZENTMAYER

### Retina and Optic Nerve

THE END RESULTS OF OPERATIONS FOR DETACHMENT OF THE RETINA WITH A FOLLOW-UP OF FIFTY-FIVE SUCCESSFUL CASES M L HINES, *Brit J Ophth* 28:575 (Nov) 1944

Hines has made a full analysis of the cases of 120 patients with detachment of the retina who were operated on by the end of 1942, with successful results in 50, or 41.66 per cent. If 49 patients who were bad risks are omitted, the percentage is 49.29. Thirteen of the patients discharged with the retina in place and a full field of vision returned at intervals varying from three weeks to six months with a history of sudden loss of vision and the retina again detached. Two patients sent out as representing failures returned later with the retina in place and a full field of vision. In 1 patient the redetachment took place three years after the operation. Further operation was unavailing. This patient was 9 years of age and had been operated on previously elsewhere, without success. Four patients had aphakia. In all of them the operation was a failure. Twenty of the series had secondary operations, with 3 successes. A definite history of trauma was elicited from 13.83 per cent. Forty per cent were myopic.

Most of the patients received surface diathermy with Weve's applicator, the current varying from 110 to 120 milliamperes, followed by diathermy puncture and removal of as much subretinal fluid as possible with a "sucker." Further analysis with respect to such factors as age, position of holes, final vision and visual field is made.

W ZENTMAYER

RETINOSIS ACCOMPANYING NIGHT BLINDNESS A MOREU, *Arch Soc oftal hispano-am* 4.115 (Jan-Feb) 1944

So-called pigmentary degeneration of the retina is not a well established nosologic entity. There are several varieties, one of which is acquired. In the beginning the condition in the retina has a physiologic basis, the anatomic changes come later.

Studies were conducted on the classic familial type. Observations were made on children with the disease, and experiments were carried out on animals.

Twenty-two children, 10 boys and 12 girls, from 10 to 18 years old, were studied. Anatomically, 2 patients presented peripheral lesions of the retina and 6 showed attenuation of the retinal arterioles. Fourteen were apparently normal. The children with anatomic lesions showed contracted fields, while the apparently healthy children exhibited changes in the threshold for dark adaptation.

Determination of the chronaxia of the retina indicated a normal reaction in the children with no anatomic lesions. This tended to prove that the factor giving rise to the phenomenon of night blindness has its seat in the layer of the rods and cones, in the choriocapillaris and in the pigment epithelium.

The first symptom of the disease in these children was night blindness, denoting that some disturbance in the metabolism of the visual purple was taking place. General physical examination showed disturbance in the endocrine-sympathetic nervous system. The vitamin A content of the blood was, however, normal.

The investigator has formulated a hypothesis for the causation of pigmentary degeneration of the retina. The beginning of the process, according to him, is due to some dysfunction of the hypothalamus. Experiments on animals partly proved his assumption.

H. F. CARRASQUILLO

### Trachoma

SULFONAMIDE THERAPY OF TRACHOMA. J. A. SENÁ, *Arch. de oftal. de Buenos Aires* 18:703 (Dec.) 1943.

The use of the sulfonamide compounds has been one of the greatest advances in the treatment of trachoma in the last fifty years. These drugs have given first place to the general treatment of the disease, with the local therapy relegated to a secondary position.

The author relates the history of the use of the sulfonamide drugs in the treatment of trachoma. He made a trial treatment of 2 patients with a severe form of the disease and concluded that the medication was effective, and since then he has continued its use. He has obtained the best results when the disease had a corneal predominance. The drug is administered by mouth and locally in the form of a 10 per cent solution of sodium sulfathiazole and a 30 per cent solution of the sodium salt of sulfacetimide. He attributes to the oral administration a striking effect on the subjective symptoms.

For the rapid disappearance of the conjunctival lesions (follicles) he still uses the copper sulfate pencil as a supplementary measure. Although he is enthusiastic over this new treatment of trachoma, he states that it is yet too early to speak of it as producing a definite cure.

H. F. CARRASQUILLO

# Society Transactions

EDITED BY DR W L BENEDICT

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NEW YORK ACADEMY OF MEDICINE, SECTION OF OPHTHALMOLOGY

Rudolf Aebli, M D, *Chairman*

Truman Boyes, M D, *Secretary*

*March 18, 1946*

INSTRUCTION HOUR

## Clinical-Pathologic Correlations in Cases of Enucleation of the Globe

DR JOSEPH LAVAL

The author correlated the clinical histories with the pathologic changes in the enucleated eyeball demonstrated in the following cases

CASE 1 —The lens was found to have been injured at operation for acute glaucoma

CASE 2 —The clinical diagnosis was melanosa sarcoma of the choroid, and examination of the eyeball showed that the sarcoma had perforated the globe and extended into the sheath of the optic nerve

CASE 3 —A patient aged 69 had been blind in one eye since the age of 18 as the result of trauma. The clinical diagnosis was phthisis bulbi, but the atrophic eyeball showed the presence of sarcoma of the choroid

CASE 4 —The clinical diagnosis was sarcoma of the choroid, and examination of the eyeball showed that the tumor had perforated the globe and a large extra-ocular mass was present

CASE 5 —The clinical diagnosis was sarcoma in the macular region, but a subretinal hemorrhage was observed on examination of the enucleated eyeball

CASE 6 —The eyeball of a patient aged 28 was enucleated for sarcoma of the macular region. The clinical diagnosis was confirmed on examination, the tumor was very small

CASE 7 —In a case of acute glaucoma examination of the eyeballs showed a melanosa sarcoma with signs of old glaucoma

CASE 8 —The eyeball was enucleated for tumor of the iris, but examination revealed a benign cyst of the stroma of the iris

CASE 9 —In a case with a history of inflammation and increased tension following operation for cataract a diagnosis of exudate in the anterior chamber was made, but examination revealed the presence of a downgrowth of epithelium

CASE 10 —In a case in which operation had been performed for congenital cataract and absolute glaucoma had then developed, twenty-nine years before, examination of the enucleated eye showed a hyaline membrane on the iris

CASE 11 —For an 18 month old child a diagnosis of endophthalmitis had been made, but microscopic examination of the eye showed glioma, which had extended into the anterior chamber

CASE 12 —For a 9 month old child a diagnosis of glioma had been made, and examination of the eyeball proved this to be correct

CASE 13 —In a child 4 years of age the mother had noticed the appearance of a "cat's eye," and a diagnosis of glioma had been made, which was verified on examination

#### REPORT OF CASES

### Removal of a Foreign Body from the Orbit with Aid of the Berman Localizer DR SAMUEL WENGER, Flushing, N Y

E S, a 5 year old boy, was struck in the right eye with the end of a small paintbrush on Jan 1, 1946 The injury was followed by pronounced swelling of the right upper lid, entirely closing the palpebral fissure On January 15, two weeks after the accident, the patient was referred to me for consultation A roentgenogram taken at this time disclosed the presence of a large intraorbital foreign body, about  $1\frac{1}{2}$  inches (3.8 cm) long which corresponded to the metallic end of the paintbrush containing the bristles There was no pain or inflammation. The eyeball was fixed and rotated downward Vision was normal

The patient was admitted to the hospital on January 16 With the child under general anesthesia, an incision was made horizontally across the upper lid just below the superior orbital rim At no time could the foreign body be seen or palpated After probing for at least half an hour, during which encapsulated pus was encountered, I inserted the tip of a Berman localizer, the foreign body was instantly located and its removal readily accomplished

The case is of interest in that there was so much difficulty in locating such an unusually large foreign body The metal was nonmagnetic, and it is felt that the results obtained with the Berman Localizer were gratifying

#### DISCUSSION

MR SAMUEL BERMAN I have here the foreign body which is the subject of this case report As you can see, it is about  $\frac{1}{8}$  inch (3 mm) in diameter and 1 inch (2.54 cm) in length, and for the purpose of this demonstration it has been attached to the thin wooden handle of the brush from which it had originally broken off Although this foreign body is of aluminum, and therefore nonmagnetic, it was readily detected with the probe of the Localizer because of its relatively large size and the fact that the incision was initially placed with sufficient accuracy to bring the probe within easy detecting range The localizer which was used in this case, and which is here demonstrated, has two indicators a meter for visual and a loudspeaker for auditory indication I shall demonstrate what happens when the probe approaches the foreign body (demonstrating) The closer the foreign body is approached, the higher the meter indicator goes, simultaneously, the tone from the loudspeaker rises in pitch The nonmagnetic foreign body demonstrated here is detected from a distance of about  $\frac{1}{4}$  inch (6 mm) In general, nonmagnetic foreign bodies of relatively small dimensions that is, spherical bodies smaller than 3 mm in diameter, occurring intraocularly will not be detected with the localizer The detecting range for larger nonmagnetic foreign bodies is from one to two times the diameter of the foreign body

The sensitivity of the Localizer to iron or steel, however, is very high the detecting range being about ten times the diameter of the foreign

body, that is, a mass 1 mm in diameter will be detected from a distance of 10 mm, and a mass 2 mm in diameter, from a distance of 20 mm

I have several samples of magnetic foreign bodies with which I shall demonstrate the use of the Localizer for foreign bodies. The one which I now have in my hand (demonstrating) is of common steel,  $\frac{1}{8}$  inch in diameter and about  $\frac{1}{4}$  inch in length. This fragment is detected from a distance of well over 1 inch. This sponge with an open slit, representing a wound in which a small foreign body has been placed, will illustrate the manner in which the Localizer is used in general surgery or in the removal of an intraorbital foreign body (demonstrating). The probe is inserted within the wound, and the tip is moved about so as to scan all the interior surfaces. The point at which the maximum response is noted indicates the position of the foreign body and determines the direction in which to proceed with further dissection.

To illustrate the use of the Localizer in work with intraocular foreign bodies, I have this artificial eye, against the inner surface of which is glued a tiny magnetic foreign body, made of violin E string wire, 0.25 mm in diameter and a 0.5 mm in length. This is about the smallest size of intraocular foreign body ordinarily encountered (demonstrating). I get a good response through the glass, which represents the average thickness of the sclera. As I move the tip of the probe along the surface, the effect varies. The point where the peak response is obtained is the point of closest approach. I shall now move the tip of the probe about 0.5 mm to one side of this point. The sound changes abruptly, although the movement is probably not visible to persons in the back of the room. This is what is termed "pinpoint" localization, expressing the high accuracy obtainable with this device.

Sterile conditions are obtained by applying a rubber jacket over the probe. This jacket is of surgical rubber and may be boiled or autoclaved. It in no way interferes with the detecting action.

For work with intraocular foreign bodies, the outer shield of the probe is generally removed, thus reducing the diameter of the tip and permitting closer approach of the sensitive element to the surface, with resulting still greater sensitivity and accuracy. The bare element is then covered only with the sterilizable rubber jacket.

DR TRUMAN L. BOYES. How does the Localizer react to lead bodies?

MR SAMUEL BERMAN. The Localizer does not react as strongly to nonmagnetic as to magnetic foreign bodies. A nonmagnetic foreign body has to be fairly large in order to produce a reaction at any appreciable distance.

DR JOSEPH LAVAL. The localization of magnetic and nonmagnetic foreign bodies was well demonstrated three years ago at Mount Sinai Hospital, in an attempt to localize a small piece of copper. A roentgenogram was of no help in deciding whether it was localized in the sclera or in the orbit.

DR ARNOLD KNAPP. How is the action with nonmagnetic foreign bodies explained?

MR SAMUEL BERMAN. In the detection of nonmagnetic foreign bodies, the reaction occurs through what is known as eddy currents.

The alternating magnetic field about the probe sets up these small currents within the mass of metal being searched for. These currents, in turn, produce local magnetic fields about the metallic mass, which react with the field of the probe and thereby cause the changes, resulting in the sound which was heard.

DR WENDELL L. HUGHES, Hempstead, N. Y. May lateral pressure on the end of the tip give a false reading when no foreign body is present?

MR. SAMUEL BERMAN: Yes. In using the instrument with the outer shield in place, lateral pressure must not exceed 1 pound (373 Gm.). Such pressure is, of course, never approached in ophthalmic work. In general surgery, however, when one is probing in a bony area, one must not use the probe as a pry or the pressure limits may be exceeded and a false response, or pressure error, be produced (demonstrating). I am now pressing against the tip of the probe with about  $\frac{1}{2}$  pound (186 Gm.) pressure, without any effect. I now increase the pressure, and a response similar to that from a foreign body is obtained. One must be especially careful when using the probe with the shield removed, as is recommended for work with intraocular foreign bodies. For such use, the bare sensitive element is covered only with the sterilizable rubber jacket to exclude dirt and moisture, and any pressure amounting to more than the barest contact against the surface of the globe may produce pressure errors. The degree of pressure error is readily determined by the operator by applying the tip of the probe to his gloved hand with approximately the same pressure as that used on the surface of the eye.

#### PAPERS OF THE EVENING

**Binasal Hemianopsia.** DR. J. IGERSCHEIMER, Boston

This paper will be published in a future issue of the ARCHIVES

#### DISCUSSION

DR. THOMAS H. JOHNSON: I regret I did not have the privilege of reading Dr. Igerscheimer's paper before his presentation.

Binasal hemianopsia is a rare finding. At the Neurological Institute of New York, my associates and I took 3,346 visual fields on patients who had neurologic disturbances, of these, 230 showed defects in the visual fields. In only 1 case was there binasal hemianopsia. I have seen only 3 cases of binasal hemianopsia in my entire medical career. In 2 of them there was no autopsy. In these 2 cases the cause of the hemianopsia was believed to be calcification of the internal carotid arteries. The diagnosis was based on roentgenologic examination and the absence of any other neurologic findings. The relation of the internal carotid arteries to the chiasm varies in different persons. Schaeffer (Some Points in the Regional Anatomy of the Optic Pathway, with Special Reference to Tumors of the Hypophysis *Anat. Rec.* 28:243, 1925), in a dissection of 125 cadavers, demonstrated that the chiasm varies in its relation to the surrounding structures. He observed that the chiasm may lie in front of, directly over or behind the hypophysis. In cases in which the chiasm is located well posteriorly the optic nerve is rather long. A slide was shown of a drawing of an aneurysm of the circle of Willis demonstrating the relation to the surrounding structures.



of the internal carotid artery as it comes from the cavernous sinus and divides into the anterior and posterior cerebral arteries. It is noted that the internal carotid arteries lie in fairly close relation to the chiasm. In persons in whom the chiasm is located well posteriorly the internal carotid artery may be in close contact with the optic nerve. The internal carotid artery is tortuous in its course and if calcified could exert pressure on the lateral sides of the nerve in some cases and on the chiasm in others.

A diagnosis of calcification of the internal carotid arteries is justified when binasal hemianopsia is present, the roentgenographic examination demonstrates evidence of calcification in the arteries and there are no contravening neurologic signs.

The third case of binasal hemianopsia I have seen was that of a boy 9 years of age, studied at the Neurologic Institute. He had binasal hemianopsia with a defect in the upper temporal fields as well. There was advanced bilateral papilledema, with greatly reduced vision. The outlook was serious, and the neurosurgeons did an exploratory operation, using the transfrontal approach. When the middle fossa was exposed, a cystlike mass, under pressure, was seen compressing the structures anteriorly. The presence of a neoplasm was not confirmed, and biopsy revealed normal brain tissue only. The fluid which was aspirated proved to be normal cerebrospinal fluid. The boy died about three weeks later, of bronchopneumonia, and autopsy revealed an astrocytoma fibrillare beneath the aqueduct of Sylvius. The tumor had grown into the lumen and practically obliterated it. The resulting internal hydrocephalus had dilated the third ventricle, causing the anterior wall to bulge into the chiasmal region. It was believed that the optic nerves were pressed against the internal carotid arteries, with consequent destruction of the lateral fibers of the nerves, thus producing the binasal hemianopsia.

The Paton-Kennedy syndrome may be explained by an expanding lesion which compresses the optic nerve on the ipsilateral side, destroying the fibers and obliterating the subdural spaces. When the lesion has grown sufficiently to produce intracranial pressure, papilledema develops on the contralateral, unobstructed side. No papilledema develops on the side of the lesion because the obliterated subdural spaces prevent the impact of the pressure against the nerve head. The scotoma in the contralateral visual field may be due to a toxin thrown off from the neoplasm or other expanding lesion.

Albright (*Bull Johns Hopkins Hosp* 44 215-245, 1929) reported 31 cases of the syndrome due to aneurysm at or near the circle of Willis in which autopsy was performed. In none had a diagnosis been made during the life of the patient. The third cranial nerve had been involved in each case, the sixth cranial nerve in 19 cases and the superior division of the fifth nerve in 24 cases.

A slide was shown of a drawing after Meyer, published in one of Cushing's papers, to demonstrate the visual centers in the occipital lobes and the optic radiations as they course through the cerebral structures. It is conceivable that there could be a lesion in each temporal lobe which would compress the lateral fibers of the optic radiations or a destructive lesion in each calcarine area, either of which could produce bilateral nasal hemianopsia. However, I have had no personal knowledge

of such a case. Therefore, in the presence of a binasal hemianopsia, one may with reasonable certainty find the lesion in the middle fossa, located in the optic nerve, near its origin, or in the chiasm proper. Lesions of the optic tract are not common, and there are so many vital structures in the immediate proximity that other serious neurologic symptoms exist when the tract is involved. A bilateral lesion is a requisite for the production of binasal hemianopsia. I cannot reconcile the visual fields in this case with an aneurysm confined to one side, and Dr Igersheimer's explanation does not seem to be altogether satisfying. I should like to ask whether he can further amplify his explanation.

DR JOSEPH IGRSHEIMER, Boston. I should like to answer Dr Johnson's question, but I am not able to explain the binasal hemianopsia in this case. I can only repeat what I tried to say before, that the optic nerve on the side opposite the aneurysm was perhaps pressed against an arteriosclerotic artery, arteriosclerosis undoubtedly was present. Or there was perhaps a local nutritional deficiency, so that most of the smaller vessels of the optic nerves and chiasm were in some way pathologic, this is just a hypothesis, however. The latter possibility would be a good subject for investigation, for not much is known about the blood supply. Such a nutritional deficiency would better explain why the visual field of the left optic nerve was regained after the exploratory operation, in which nothing was done, whereas if an arteriosclerotic vessel had been pressing against the left optic nerve it is not clear why the operation should have changed this.

**Intraocular Hemorrhage Following Extraction of Cataract.** DR W C OWENS and DR W F HUGHES JR, Baltimore

This paper will be published in full in a future issue of the ARCHIVES

#### DISCUSSION

DR WALTER S ATKINSON, Watertown, N Y. Dr Owens and Dr Hughes, in their excellent presentation, have crystallized the views concerning postoperative hemorrhage following cataract extraction.

The low percentage of hemorrhages in the series of cases which they have analyzed is most commendable. In a great measure this can be attributed to operative skill and improved technic. Their suggestion, however, that "the difference in the reported incidence of postoperative hemorrhage is due to variations in definition" is logical. It might explain the low incidence, 7.7 per cent, of hemorrhages in the early cases, in which no sutures were used, as compared with that of 12 to 13 per cent in the series in which conjunctival sutures or one corneoscleral suture was used.

It is my impression that a number of years ago, during the period when sutures were not used, many small hemorrhages were not recorded, as they were considered as of no consequence and apparently did little, or no, harm. Then, too, in the present cases the percentage of hemorrhages for the whole series has unquestionably been lowered by the small number of hemorrhages that have occurred since the adoption of the technic to obtain firm closure with avascular healing.

I hope Dr Owens will describe the corneal section which he refers to as a shallow one with avascular healing. When such a section is used, are the hemorrhages smaller, with less visual loss?

In my experience of the past few years, the use of a corneal section with firm closure has greatly reduced the amount of bleeding, although the number of postoperative hemorrhages per hundred cases is larger than that in the Wilmer series. This, again, may be partly explained by the "variation in definition" mentioned by Dr Owens. For some time I have recorded as postoperative hemorrhages all those in which any blood was seen in the anterior chamber at any dressing, since it does not seem practical for each operator to decide which hemorrhages are large enough to record. The notable decrease in the number of hemorrhages, 13.3 per cent, in the group with one corneoscleral suture as compared with the incidence of 4.7 per cent in the group in which two corneoscleral sutures were used is particularly striking. Was the same type of section employed in the two groups?

The authors report hemorrhages following the removal of corneoscleral sutures in 3.6 per cent of their cases, which leaves only about 1 per cent of the hemorrhages in the last series of 558 cases attributable to other causes. If the percentage of hemorrhages following the removal of sutures could be lowered, the problem of postoperative hemorrhage would be near solution.

The conclusion in regard to the influence of general medical conditions as a cause of postoperative hemorrhage is in accord with my experience. Frequently a hemorrhage can be accounted for by a poorly placed section which has been insecurely closed.

In my last 300 consecutive cases of cataract extraction, which include instances of complicated cataracts, there were 34 postoperative hemorrhages. One patient died of a cerebral hemorrhage before leaving the hospital. The others obtained vision of 20/25 or better. Therefore, I have felt that while postoperative hemorrhage is an annoying complication, which may prolong the patient's stay in the hospital, it is not a serious one.

The excellent presentation of Dr Owens and Dr Hughes has strengthened my conviction that an accurate and firm closure of a corneal section will practically eliminate postoperative hemorrhage.

DR FRANKLIN BRACKEN. I have little to add to this excellent paper. I am convinced that firm closure of the wound is the best defense against hemorrhages and that it has greatly reduced them in number and size. Hemorrhage causes no great trouble in my experience, does not greatly affect the vision and seldom makes any difference in the final result. The patient's hospitalization may be prolonged, and staining of the cornea occasionally occurs, but I have seen normal vision eventually result in cases of corneal staining which endured for more than a year.

DR ARNOLD KNAPP. Drs Owens and Hughes have made a valuable presentation, for it demonstrates that the cause of hemorrhage is not systemic or general but is a local one which can be present in any type of case, that it can be remedied by an improved operative method is particularly valuable.

DR CLYDE E. MCDANNALD. I know of surgeons who do a phlebotomy to prevent hemorrhage. I should like to ask the authors whether they performed phlebotomy on any of these patients before operation.

I never saw a case in which that operation was resorted to, but I know of good surgeons who employ it

DR W C OWENS, Baltimore Phlebotomy was not performed in any of the cases of this series There have been reports in the literature on the relation of phlebotomy to the occurrence of postoperative hemorrhage Carle compared cases of vascular hypertension in which phlebotomy was performed with cases of vascular hypertension in which no phlebotomy was performed He found no significant difference in the incidence of postoperative hemorrhage in these two groups

The following technic was employed in the cases with two corneoscleral sutures and is the technic used at the present time After production of akinesia and a retrobulbar injection, a lid speculum is inserted, and a traction suture is placed in the superior rectus muscle An incision for a conjunctival flap, measuring 3 to 4 mm, is made from 3 to 9 o'clock and carried down to the limbus to the point of transition between conjunctival and corneal epithelium This point is about 1.75 to 2 mm from the root of the iris A partial incision is then made halfway through the thickness of the limbus at an angle of 10 to 15 degrees from the perpendicular Into this partial incision are placed two corneoscleral sutures, at 1 and 11 o'clock A Graefe knife is used to make the section, which comes out in the base of the partial incision previously made The necessity that the Graefe knife follow the partial incision, carefully placed beforehand, insures a section in the exact position desired—well forward in relatively avascular tissue

In the cases with conjunctival sutures and in a few cases with only one corneoscleral suture, the sections were more posterior, and therefore in more vascular tissue

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Rudolf Aebli, M D, Chairman

Truman Boyes, M D, Secretary

April 15, 1946

#### INSTRUCTION HOUR

#### Wrong Glasses From the Right Prescription. MR AUREL E MANGOLD

In this discussion the speaker stressed the importance of proper fitting of ophthalmic lenses, explaining how and why improper adjustment may impair the results of an expert refraction He dealt with correct methods of measuring interpupillary distances, compensation for vertical imbalances in anisometropia, vertex distances and their effects on lenses for cataract and on high corrective lenses He also included consideration of the importance of lens forms as related to aniseikonia, mechanical factors and difficulties encountered with lenses for aphakia and high dioptric prescriptions, and critical factors in the selection of lenses for such conditions The use of the lensometer, the lens clock and neutralization as methods of checking finished lenses and the analysis of lens forms in relation to the patient's refractive errors were emphasized A suggested routine for checking lenses, by themselves and in their relation to the patient and his symptoms, was also presented

## REPORTS OF CASES

**"Soft Glaucoma" and Calcification of the Internal Carotid Arteries**  
DR JOHN M McLEAN and DR BRONSON S RAY

This paper will be published in full in a future issue of the ARCHIVES

## DISCUSSION

DR BRONSON RAY It is all very well to suggest a possible mechanism for this ophthalmologic problem. We should be much more gratified to be able to suggest something to do about it. The rather difficult situation in the case we presented, and in others like it, is obvious. Yet it may be that there is something to be accomplished by a procedure which we hope we may try at another time, namely, the decompression of the optic nerve in its canal by removal of the roof of the canal. In a situation such as Dr McLean has shown the nerve is virtually held immobile as it enters its canal, and at that very point it receives its greatest insult from the artery. Theoretically, it seems to me if one could unroof the canal and let the nerve be displaced upward it might have a better chance of survival in the circumstances. This, I realize, is complete speculation, and perhaps unwarranted wishful thinking. However, if ophthalmologists are to be enthusiastic in finding a cause for conditions such as this, they ought to show a little more enthusiasm in doing something about it.

DR ARNOLD KNAPP The authors' case corresponds to those described in the older literature as instances of atrophy of the optic nerve of arteriosclerotic origin (Otto, R. Untersuchungen über Sehnenvenenveränderungen bei Arteriosclerose, Berlin, Julius Springer, 1893). This was before the days of roentgen rays, and the diagnosis was made at necropsy. On the other hand, the cases which are now associated with sclerosis of the basal arteries are, I think, different. The altitudinal field defect, while characteristic, is not always present, the cupping of the optic nerve is distinct, and the intraocular tension is always low. Calcification of the basal vessels is not always recognizable on roentgenologic examination, but a vascular disturbance of the optic nerve is assumed to be present in all cases.

DR WENDELL L HUGHES May I ask Dr Ray whether he thinks it might be possible to unroof the canal of the optic nerve and insert fascia around the carotid artery in that area, introducing it between the artery and the nerve, in order to cushion the shock of the pulsation of the artery against the nerve?

DR CLYDE E McDANNALD I should like to ask whether any method is known which can be employed in decalcification in these cases. I ask this because I had in my office this morning a man who came first with disciform keratitis. Now, after three or four weeks, he has a spider-like opacity, and it looks very much like a calcification. He said that he had had two calcified nodes removed surgically from his elbows and asked whether there is any method of treatment which will remove calcified areas from the body.

DR BRONSON RAY The optic nerve canal is a rather confined place in which to work, and one is continually aware of the danger of traumatizing the nerve by undue manipulation. Even removal of the roof

of the canal might be fraught with hazard. But if a piece of fascia were to be introduced between the vessel and the nerve, it might counteract whatever benefit would accrue from releasing the nerve, in other words, the fascia might take up more space than was justified.

DR JOHN MCLEAN. Dr McDannald, I do not pretend to be a chemist or an authority on decalcification, and I think I had better not answer your question.

In reply to Dr Knapp's comments. I was impressed, on reviewing his two papers on the subject, by the extreme similarity of the clinical pictures and the great similarity of the visual fields in my case and in the cases which he originally reported, particularly those in his first paper. Of course, the operative observations were very different from those to be expected from his roentgenograms, but we have an equal basis for comparison. I carefully compared the fields in my case with field after field in the 10 cases Dr Knapp reported, and I was impressed, not by the differences, but by the similarity. With regard to cupping of the optic nerve and the diagnosis of pseudoglaucoma, I should like to say again that this patient was examined, and the diagnosis of pseudoglaucoma, or "soft glaucoma," made, by a fair number of ophthalmologists, over a dozen, some in this city and some in places outside New York, there was a slightly smaller number who disagreed with the diagnosis, but the disks resembled closely enough the picture of pseudoglaucoma to suggest the diagnosis to so many.

**Lipemia Retinalis.** DR F L PHILIP KOCH (by invitation) and DR PAUL S STRONG (by invitation), New York

This paper will be published in full in the ARCHIVES

#### DISCUSSION

DR LUDWIG VON SALLMANN. I should like to ask Dr Koch whether he considers examination under red-free light of value in the diagnosis of retinal lipemia, since a granular current in the retinal vessels may be detected with this method in an early stage of the condition.

DR F L PHILIP KOCH. With regard to Dr von Sallmann's question concerning examination under red-free light, we have not made such a study. It did not occur to us to study the eyegrounds from that point of view or to determine the appearance of the fundi under red-free light. The contrast was much more striking with respect to the lack of coloration than it was at a later date, that is, it was much more striking at first than when the color returned more nearly to normal.

**Ophthalmoscopic Changes Associated With Essential Hypertension as a Guide to Sympathectomy.** DR MARTIN COHEN

The paper will appear in full in a future issue of the ARCHIVES

#### DISCUSSION

DR HERMAN O MOSENTHAL. We have heard the opinions of one of the wisest of all ophthalmologists on a timely subject. He finds that sympathectomy relieves many of the changes in the fundus occurring

with essential hypertension. The close observation of 90 patients before and after operation, during their long period of hospitalization, is an arduous task, and we are greatly indebted to Dr. Cohen for the valuable records he has assembled.

Many internists and ophthalmologists have stressed the idea that the retinal lesions are the most important sign of hypertension, as a guide both to therapy and to prognosis. It is with gratification that I quote Dr. Cohen: "A definite prognosis is not possible from the findings in the fundus alone, as the prognosis may be influenced by pathologic changes in other organs." Considering that 60 per cent of the many patients with hypertension die of cardiac failure and that only a comparative few suffer visual impairment, the truth of Dr. Cohen's statement is apparent.

Also, I agree with Dr. Cohen that the eyegrounds are the best visible guide to the condition of the systemic blood vessels. There can be no doubt of the truth of that statement. However, of 22 patients with normal fundi in Dr. Cohen's series, biopsy revealed normal kidneys in only 3, while 19 had nephrosclerosis. The pathologic condition of the kidneys, therefore, is often a more delicate index of the effects of hypertension than is the appearance of the retina.

With these reservations in mind, let us look at the positive indications. Dr. Cohen's observations show that retinal hemorrhages, exudates and vasospasm will disappear after sympathectomy. This fact is of great value as a guide to the advisability of performing sympathectomy. In some instances hypertension exerts its influence on the retina in a selective, devastating fashion. Such lesions may be relieved by sympathectomy.

Dr. Hinton performed sympathectomy in 2 young men who were incapacitated through loss of vision. They were both nephritic. One had normal renal function, in the other the urea nitrogen of the blood was distinctly raised. Nephritis is considered a contraindication to the performance of sympathectomy. However, the operation resulted in complete restoration of vision in these 2 patients. They were able to resume work, one as a railway express clerk and the other in a defense plant. Within about a year coronary thrombosis and uremia closed the picture for these men. Nevertheless, one year of untrammelled living was surely worth the price.

The strain imposed on the arteries and arterioles by the hypertension is the cause of arterial and arteriolar changes. The resulting vasospasm, hemorrhages and exudates are reversible, while arteriosclerosis is not, as has been stressed by Dr. Cohen. Favorable effects come about whenever the blood pressure is lowered. The question arises: What is the most successful method of reducing arterial hypertension? Dr. Cohen has mentioned that sedation and rest often accomplish a great deal. I hope that the title of this paper does not imply that sympathectomy is the method of choice. This operation, to my mind, is distinctly in the experimental stage and is far from being a panacea for the hypertensive state.

I recall the disfavor incurred by those of us who were skeptical about the value of nephro-omentopexy and the use of renal extracts. I trust that the unbelievers may be proved wrong, but for the present

I am among those who are doubtful as to the wisdom of the extensive application of sympathectomy in cases of hypertensive disease

I shall cite the results in 3 cases of hypertension to show that there is no single formula for success in the treatment of this disease and that improvement in the fundic changes and lowering of the blood pressure may be achieved by many different means

A minister, aged 43, was seen in May 1929. He was said to have a hopeless case of uremia. He was weak to the point of exhaustion. The blood pressure was 190 systolic and 120 diastolic, the hemoglobin 54 per cent, the red blood cell count 3,110,000 and the urea nitrogen content of the blood 38 mg per hundred cubic centimeters. Vision was impaired because of retinitis. The malnutrition had been engendered, in part at least, by a low protein diet. He was given three transfusions totaling 2,500 cc of blood and was allowed a high protein diet. After this treatment the blood count became normal, the blood pressure dropped to 154 systolic and 100 diastolic, the retinitis disappeared and vision was restored, his energy revived, and he resumed preaching and attended football games. Presumably, his tissues had been injured by semistarvation. Proper nutrition reversed his condition in many respects. Two and one-half years later there was an exacerbation of the hypertension, and he died of cardiac failure. This record is fully as good as those of the 2 patients with nephritis subjected to sympathectomy previously cited.

A housewife aged 58 had loss of vision because of hemorrhagic retinitis associated with severe diabetes and a blood pressure of 238 systolic and 140 diastolic. Control of the diabetes, complete rest in bed and a low caloric diet promoted absorption of the hemorrhages. Six months later vision was again impaired because of recurrence of the retinal hemorrhages. The same measures were again effective. The blood pressure remained constantly high. Thorough relaxation and an anti-obesity diet proved satisfactory in this case, the direct opposite of the therapy used in the first case.

Mrs M, a teacher aged 42, on Dec 8, 1945 had a blood pressure of 196 systolic and 128 diastolic, one week later it was 194 systolic and 124 diastolic. The blood pressure seemed to be permanently elevated. Within another week the blood pressure dropped to 166 systolic and 110 diastolic and subsequently to 136 systolic and 94 diastolic, at about which level it has remained for four months. She has kept on with her exacting work and is subject to inescapable home worries. In addition to an antiobesity diet, resulting in a loss of weight of 26 pounds (11.8 Kg), symptomatic medication was prescribed. How such a result was accomplished I do not know, but the fact remains that gratifying changes in blood pressure were achieved by simple means, without resort to specific remedies or operation.

DR J WILLIAM HINTON. I am at a loss in discussing this paper because I can agree with some of the points that Dr Cohen has stressed, one of which is, if I understood him correctly, that the changes in the fundus are perhaps the best guide in selection of patients who will respond favorably to thoracolumbar sympathectomy, and another guide is in the grouping of these ocular changes. I am ready to admit that I am not competent to evaluate changes in the fundus and have to take the opinion of those who really know. It will be recalled that 23 of the patients in Dr Cohen's series were reported normal, the cases in this series do not represent consecutive cases; they represent only 90 cases out of about 250 in which operation was performed. Some of the patients had complete ophthalmologic studies before their entry



into the hospital, and they were not restudied, so Dr Cohen's series represents to a certain degree a cross section of the larger group. The normal findings in the fundus are upsetting, for I can assure you that, aside from the eyes, these patients were far from normal, and that in itself is confusing in selecting patients with respect to the seriousness of the operation. Recently I saw a patient who had had two attacks of coronary disease. She had been treated by an excellent cardiologist, and he felt that she should have an operation. She was normal in every other sense and had recovered from the coronary disease. Her eyegrounds were of group 1 type, and she felt that for this reason she was a safe risk. From my point of view, it is dangerous to operate on a patient who has had two attacks of coronary thrombosis, and if one relies on the eyegrounds one will be misled as to the underlying arteriolar sclerosis in the brain, coronary arteries and kidneys. The good results speak for themselves, the difficult thing is to evaluate the failures, and it is very interesting to correlate all the data available in order to decide on whom to operate and whom to exclude. The over-all mortality for the 227 patients operated on during the past four years, which means the mortality for patients in and out of the hospital to date is 26, or 11.5 per cent. Using the classification of Keith, Wagner and Barker based on the eyegrounds, one finds that 30 per cent of group 1 are dead in three years, and at the end of six years the mortality is still only 30 per cent. For group 2 the mortality is 38 per cent for three years and the same for five years. For group 3 the mortality is 78 per cent after three years, and for group 4 it is 94 per cent. It is obvious that the patients in groups 3 and 4 have had serious organic disease, in the heart, cerebral vessels or kidneys. This gives an index as to what will happen to patients falling in group 4. My colleagues and I have 20 patients in group 4 who have been operated on and followed for six months to three years. Eleven are alive and well, a proportion which compares favorably with the figures of Keith, Wagener and Barker.

In Dr Cohen's series, 23 of the patients had normal eyes and 43 mild changes, that means that 73.3 per cent of the 90 patients had minimal ocular changes, but 80 per cent of these patients were actually critically ill with advanced essential hypertension. Hence, the eyegrounds are obviously of little aid in selection of hypertensive patients, both as to their ability to stand operation and as an index as to the prognosis after operation. One can be misled if one follows the findings in the eyegrounds too literally. In reviewing the failures, I have found some interesting figures. Perhaps the most accurate clinical information is obtained from the sodium amytal test. That test must be done accurately. One cannot have one resident doing a few tests and another a few and rely on the results. For the past fifteen to sixteen months we have had a nurse technician doing nothing but these sodium amytal tests, and the results are fairly accurate. We have found that the patients whose diastolic pressure does not fall below 100 are the ones in whom we will get poor results. For practically all patients whose diastolic pressure falls below 100 the results have been satisfactory, with practically no deaths in or out of the hospital. That, from the surgical point of view, is most important, it means one has an index in selection of these patients.

In spite of the knowledge that the internists have, they cannot exclude some of the patients who have early renal disease. The urea clearance and concentration tests are satisfactory, the blood chemistry may be normal, but uremia develops, with a urea nitrogen value of 60 to 70, or even 100, mg per hundred cubic centimeters and a creatinine of 10, 12, 15 or 16 mg and a nonprotein nitrogen value which is much bigger. So far as I have been able to see, there is no satisfactory test that will rule out early renal disease. It is obvious that if the surgeon knew there was so much renal damage he would not operate. Patients with severe renal damage will not be helped by thoracolumbar sympathectomy. After one analyzes all the data, from the renal function tests, the electrocardiograms, etc., one is still in a quandary as to whether the patient will stand the operation and, if he stands it, whether the result will be good.

We have classified patients as those who were 50 years of age and those who were older. Some of the best results we have had were in persons over 50. Of 34 patients above 50, 2 were over 60 and 7 were between 55 and 60 and in two thirds of this group the results were good.

Twenty-four patients had type 4 changes in the eyegrounds. If one other organ is seriously involved, that is if there is severe cardiac, renal or cerebral damage with type 4 changes in the fundus, there is a 50-50 chance of improvement. Of 4 patients with changes in the eyegrounds of type 4 with no evidence of involvement of any other organ, all improved. If the patient has two organs involved other than the eyes, he has little chance of being helped by sympathectomy. We found that of 74 patients with one organ involved and fairly extensive changes in the eyegrounds, 50 were notably improved. Twenty-six patients died, and of these, if the changes in the eyes, kidneys, heart and brain are evaluated on the basis of + to ++++, with a total of 16 ++++ grades, it was found that 15 patients had 12 ++++ grades out of 16 such grades, and those patients should not have been operated on. The other patients who died had from 8 to 5 + grades or less, and operation seemed indicated.

The clinical impression I got from these patients is that the patients with encephalopathy do the worst. I am not speaking of persons who have had strokes, some of them do very well, I mean the patients who have had a period of unconsciousness of three to five minutes, or they are irritable, they grope for words, their memory is poor, which means they have fairly advanced cerebral arteriolar sclerosis, and we have found this group of patients, although they may have good renal function and good electrocardiograms, are the ones who will die of a cerebral thrombosis or hemorrhage.

To sum up. The eyegrounds are definitely an aid in selection of patients, but they represent only one phase of the problem. Seventy-six per cent of the patients in this series had histologic evidence of renal disease. It is evident, then, that the renal disease precedes arteriolar changes of the retinal vessels when, according to Dr. Cohen's observation, 73.5 per cent had minimal changes or normal eyegrounds.

DR FRANK A. VESEY. It was a pleasure to listen to these excellent presentations, and I enjoyed most those of Dr. Cohen and Dr. Mosenthal. Dr. Hinton presented his views ably, and they can be discussed with

the papers of the other two. I was glad that Dr. Cohen did not choose to discuss the Wagener-Keith-Barker classification. No matter how fashionable it is today, it is rather artificial, looked at from the ophthalmologic angle. The first two groups can well be interpreted as normal, and I am glad that Dr. Cohen spoke of mild, moderate and severe changes and of malignant hypertensive retinopathy.

Dr. Cohen pointed to an artery on one of his slides, saying that this artery, although attenuated, cut in two the underlying vein. Such arteries are not really attenuated, in fact, they are thickened. But hyaline degeneration and thickening do not always make the arterial walls visible. In most cases they remain entirely transparent, and the arteries seem attenuated on account of the narrowed lumen. The underlying vein seems interrupted by the concealment.

As to the merit of sympathectomy, I think it should at best be regarded as palliative treatment. I have seen cases in which there was no beneficial result and others in which there was temporary subjective improvement, but I was not lucky enough to see, or even to read about, one in which an unbiased observer could testify to a real, substantial improvement.

Dr. Cohen says that the fundus picture is a good indicator of the real condition of the patient. Dr. Hinton does not believe that this is so. I think most of us here agree with Dr. Cohen. If the underlying hypertensive disease is severe enough to cause visible changes in the retina, the other organs, especially the kidneys and the brain, will invariably present changes of an even greater degree—so much so that if a definite retinopathy is visible and can be so diagnosed the life expectancy of the patient is not more than three years. Of course, some such patients may go on longer, but others will fall victim to a cerebral catastrophe or uremia much sooner.

Dr. Hinton said that the best patients for operation are those who display no retinopathy. These are the patients who can carry on for decades with general medical treatment, and sympathectomy is superfluous.

DR. F. L. PHILIP KOCH. Dr. Cohen has presented this subject interestingly. I wish to ask him several questions concerning basic intraocular physiology and pathology. Does he believe that there exists any justification for retention of the term "torquosity" with reference to the retinal arterioles in hypertensive disease? Does he recognize the dynamism inherent in the progression of hypertensive disease from normality through the alterations attendant on abnormal vascular physiology of the arterioles to the progressive phases of organic arteriolar changes, represented ophthalmoscopically by the so-called copper wire and silver wire appearance? Does he recognize that statistical evaluation of postoperative data on occasion has been conducted with more enthusiasm than objectivity and that it has failed to recognize the importance of the degree, or intensity, not only of the attenuation of retinal arterioles but also of the sclerosis, as well as its origin?

It will be recalled that in the early days of ophthalmoscopy the indirect method frequently was used, but even the most careful observers failed, under the standards of illumination then prevalent, to distinguish sufficiently between the pathologic vascular alterations of one entity as

compared with those of others, as they are known today, to assist the internists in differentiating any one hypertensive syndrome complex from any other. This statement does not hold true uniformly, but its basic accuracy is attested by the retention, even today, of the term "albuminuric retinitis" in some communities in this country and elsewhere. This term, although no longer in reputable use, is one of the numerous hold-overs of nomenclature of an earlier period, during which it came to be recognized that "cardiovascular-renal" disease was not a single disease but represented a clinical *pot pourri*, which was comprised of many ingredients in almost infinite combination.

The concept of arteriolar, in contradistinction to arterial, physiology and pathology gradually gained supporters. The occurrence of atheromatous changes elsewhere than in the great vessels was recognized, and its importance was established in geriatrics. It was acknowledged that there existed a difference with respect to a man's usefulness as a citizen and his life expectancy on an actuarial basis and that differentiation must be made between the chronic and the more severe phases of vascular disease, particularly with reference to hypertensive disease. Ophthalmoscopic diagnostic criteria tended to become increasingly important, but these could not be accorded their full stature unless, and if, some of the earlier phraseology was discarded. "Fortuosity," for example, is a term that should be used with great care. It implies a decrease in elasticity of the arteriolar and arterial walls. This is provable in the laboratory. On the other hand, it connotes a diminution in the ability of the wall to undergo constriction. Perusal of the older literature will reveal the fact that indirect ophthalmoscopy accentuated whatever waviness of the vasculature was present. Many of the very early observers, who, a half-century before the routine use of the sphygmomanometer, tended to believe that cardiovascular-renal disease was simply cardiovascular-renal disease, understandably were somewhat responsible for the terminology that many ophthalmologists still use in describing the eyegrounds. It is this unfortunate tendency to overlook the basic reasons for the pathologic changes observed that leads many ophthalmologists to cling to descriptive terminology that no longer has any modern clinical usefulness, except in a historical-descriptive sense. It is the same tendency, deplorably, that militates against consistently accurate interpretation of changes in the eyegrounds that we observe.

It is especially important that interpretations be as accurate as possible when one is determining whether to advise a patient to undergo surgical treatment for the relief of essential hypertension. It has been shown by Wagener and his group and by others that in the main the less intense the arteriolar sclerosis in a patient with established hypertension, the more likely is he to derive benefit from sympathectomy, and the more advanced the sclerosis, the less likely is he to obtain relief, although severe cephalgia probably will decrease in approximately one third of all cases. It is unreasonable to suppose that sympathectomy will be beneficial where generalized atheromatosis has coexisted with essential hypertension or has been present prior to the onset of increased diastolic systemic blood pressure.

DR MARTIN COHEN. I have examined about 34 patients with malignant essential hypertension with all the clinical manifestations and have studied sections of autopsy material, including serial sections, and

in most cases I found malignant nephrosclerosis. Malignant nephrosclerosis is a pathologic diagnosis. In cases of neuroretinopathy with edema of the disk, even partial edema, and increased pressure, one will find pathologic evidence in the kidney of malignant nephrosclerosis, all the blood vessel walls will be fibrillated, the lumen of the vessels will be encroached on, and theastica will be separated and split. Since in cases of malignant essential hypertension, with or without papilledema, the kidney shows malignant nephrosclerosis, I think the term malignant essential hypertension with or without papilledema should be included in the diagnosis. In one of the articles cited a case of malignant hypertension with neuroretinopathy was described.

In regard to the case of atherosclerosis of which Dr. Hinton speaks, the lesion is not arteriolar, it affects the larger blood vessels, such as the aorta or some of the cerebral basilar vessels, where one sees plaques, no plaques are seen in any arteriolar vessel.

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## News and Notes

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### GENERAL NEWS

**Howe Lecture in Ophthalmology**—Prof. William John Brownlow Riddell, fellow of the Royal Faculty of Physicians and Surgeons, and dean of medicine at Glasgow University, will give the Howe Lecture in Ophthalmology on "Heredity and Variation in Clinical Ophthalmology" at the Harvard Medical School on Tuesday Nov. 19, 1946.

## Book Reviews

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**The Fundamental Colour Sensations in Man's Colour Sense** By Gustav F. Gothlin Pp 76, with 21 illustrations in black and white  
Uppsala Almquist & Wiksells, 1943

This monograph, which is the authorized English translation of the original treatise in Swedish, will appeal to the student of color vision and color vision theory more than to the ophthalmologist. It includes a report on experimental work previously published by the author which deals with color responses particularly in the yellow and indigo regions of the spectrum. These data together with historical and critical observations, form the framework of Gothlin's thesis that the fundamental color sensations in man's color sense are red, green and blue, that yellow and violet are not fundamental colors—points of controversy since before the days of Thomas Young. A fundamental color sensation is defined by Gothlin as the sensation that would be produced by any one of the retinal processes alone, assuming it could occur alone.

Yellow, he contends, is a sensation arising from the simultaneous effect of impulses from the receptors for red and green. This conclusion is drawn from his experiments which show that the position of pure yellow in the spectrum varies among persons having normal trichromatic vision, that the range of pure yellow in the spectrum is very narrow and that there are individual differences in the Rayleigh equation which are not satisfactorily explained by assuming individual variation in macular pigment. These phenomena are best explained by assuming (page 10) "an individually varying proportion of the number of receptors for red and for green." As further evidence against the supposition of yellow as a fundamental color he cites the binocular fusion of red and green to give yellow (claimed by Hering and Trendelenburg, denied by Rochat) and the extraordinary narrowness of the spectral zone for yellow shown in hue discrimination curves.

Violet, the author contends, is a sensation arising from the simultaneous effect of impulses from the receptors for blue and red. He reviews critically previous arguments in favor of violet as the short wave fundamental color, which were based mainly on color mixture data and studies of the color vision in cases of congenital tritanopia. From his detailed analysis of these rare cases of defective color vision Gothlin concludes (page 67) "that they belong to two categories. The cases belonging to one group are blue-blind but have colour sensations from the violet part of the spectrum. Those belonging to the second group are both violet and blue-blind. In the latter group a simultaneous weakening in the perception of long-wave red was observed." To the reviewer, this section of Gothlin's book is the most interesting. Reported cases of congenital tritanopia are few and not readily accessible. This compilation has therefore considerable value.

The author's experimental evidence in favor of blue and against violet as a fundamental color is based on his attempt to separate the

blue and red components in violet in persons with normal color vision. A series of experiments on the threshold energies for the appearance of color in spectral light of wavelengths ranging from 430 to 460 millimicrons shows that for most of his observers the color was first identified as blue. Only with greater energy of light was the red component identified. No observer reported an appearance of violet or green prior to the appearance of blue. Gothlin concludes (page 67) "that blue must have its own receptors and be a fundamental colour, but that indigo—in one case also proved for violet of wave-length 425 mu—arises from the fusion of impulses from blue and red receptors."

Considerable space is devoted to the development of Gothlin's three component theory, based on red, green and blue as fundamental colors. He holds (page 70) "that every impulse from the retinal receptors to a colour sensation is necessarily combined with a certain degree of central inhibition of the complementary colour in the same area, the degree of this inhibition being bounded by a certain law." Red plus green yields yellow and yellow plus blue yields white, by a mechanism taken to be an inhibitory action in the central nervous system. The theory is illustrated with a compound balance model. While containing elements derived from the classic Young-Helmholtz and Hering theories, his thesis is most reminiscent of the Ladd-Franklin theory (1892), although the similarity is not mentioned by him.

GERTRUDE RAND

**Collected Reprints from the Wilmer Ophthalmological Institute of  
the Johns Hopkins University and Hospital July 1942-July 1945  
Volume 7 Pp 134 Baltimore, 1945**

The reprints of the articles written by members of the Wilmer Ophthalmological Institute during the period from July 1942 to July 1945 have now been collected in a bound volume, making volume 7 of the series. There are 61 titles of reprints and 6 titles of articles not reprinted in this volume.

The articles treat a large variety of subjects, which represent additions to knowledge in practically every branch of the now broadening field of ophthalmology and are witness to the interest and industry of the members of the Wilmer staff, under the stimulating guidance of their director.

ARNOLD KNAPP

## DETACHMENT OF THE RETINA

### Pathologic and Therapeutic Considerations

H. ARRUGA, M.D.

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Translated by Charles A. Perera, M.D.

NEW YORK

GONIN'S demonstration that retinal detachment is cured by sealing the retinal tears clarified and oriented the previously vague conceptions of the etiology, pathogenesis and therapy of this process. Fundamental concepts have been accepted as basic, even though some of these concepts have been modified during the past fifteen years as a result of the examination of a large number of patients with much greater care than was observed before the time of Gonin. All are aware that studies of the fundus used to involve the posterior pole of the eyeball with much less attention on the details of the periphery of the retina than is now given. Few oculists knew that tears are present in the great majority of cases, and in some cases of detachment the lesion was diagnosed as some other condition.

Detailed studies of the ocular fundus and histologic examinations of enucleated eyeballs have demonstrated that in cases of idiopathic detachment the retina is much altered. Indeed, it is strange that retinal detachment is not of more frequent occurrence. Some eyes which have a congenital predisposition to detachment reveal ophthalmoscopic evidence of atrophy and cystoid degeneration. In histologic studies, atrophic and degenerative lesions are seen to reduce the thickness of the retina to one-third normal, at times over large areas. Thus, for each patient with a detached retina there are many others who are predisposed to the same condition. The only factor which is lacking is the adhesion of the retina to the framework of the vitreous, which elevates the retina as a result of jerks or ocular movements. Even in a certain number of these patients, many more than was at first believed, the retina does not detach even though a hole is present in this membrane for a long time. Such a condition was previously considered a rarity, but if the retinas are examined with great care it is encountered more

Presented before the Second Pan-American Congress of Ophthalmology, Montevideo, Uruguay, Nov 26, 1945



frequently During the past eighteen years of my professional practice I have observed more than 40 cases of retinal holes without detachment

#### PATHOLOGIC CONSIDERATIONS

In order that the retina may detach, the margins of the tear must invert slightly toward the interior of the eye, so that with movements of the eyeball the vitreous strikes against them This destroys the framework of the vitreous, which passes behind the retina The elevation of the margins of the retinal hole is facilitated by postinflammatory, degenerative or senile retraction of the framework of the vitreous

It is known that the retina does not detach if it is adherent to the choroid as well as to the framework of the vitreous For this reason, chronic and degenerative processes are more likely to predispose to retinal detachment than are intense chorioretinal inflammatory processes Certain acute lesions, such as retinal periphlebitis, exudative choroiditis, von Hippel-Lagleyze disease and albuminuric retinitis, are exceptions With such lesions rents are usually not present, but when they occur they indicate a previous adhesion between retina and choroid, not between vitreous and retina Macular holes come into this category

*Trauma*—Trauma as the determinate cause of retinal detachment does not have the important role which has been conceded to it in the past In the first place, retinas do not detach unless they are diseased, except after extensive traumatism, secondly, many times there is no real antecedent trauma, and, lastly, ocular trauma is relatively infrequent as a cause of detachment More frequent causes are a blow on the cranium, a fall on the heels, sneezing, coughing and, above all, excessive stooping This last mechanism is very frequent as a cause of detachment, especially in patients who have been operated on for cataract It concerns persons who stoop to remove or put on footwear, or persons who have been in a stooping position for some time while gardening, whether watering, digging or weeding, or persons who are obliged to stoop frequently in their work, or who occasionally pick up objects from the floor, etc

It is therefore advisable to warn persons who are predisposed to detachment of the retina (patients who have had a cataract operation, especially those who were myopic) to avoid stooping, to place the foot on a chair when putting on the shoes, to use a long-handled tool in gardening, to kneel down in picking up an object from the ground, etc

*Pathogenesis*—The fundamental concept of the movements of the eyes as the factor which initiates and increases the detachment is becoming more definite, but the distinct clinical types of the disease and, above all, the varieties of its evolution show that other factors are also important

Actually, all have seen cases of recent detachment with extensive bulging which flattens into place in one or two days of rest in bed and bandaging. In other cases of equally fresh detachment with but little bulging of the detached retina, there is little, if any, improvement with repose. One known factor of influence in these cases is the size of the retinal rent. When the tear is small, there is rapid resorption of the subretinal fluid, when the hole is large, resorption is slow. With the cases of extensive tears belong those with dissections, which improve little, or not at all, with repose, even though the hole may not be large.

The rapidity with which the retina tears is of great prognostic value. If the holes are small and do not enlarge, there is evidence that the adhesions between vitreous and retina are not large, and the prognosis is good. On the other hand, the rapid formation of large tears indicates extreme friability of the retina or the existence of extensive adhesions between retina and vitreous, rendering treatment ineffective.

#### THE RAPIDITY WITH WHICH THE RETINA TEARS IS OF GREAT PROGNOSTIC VALUE

The factor of time, which used to be considered of such importance and which enhanced the urgency of operation, is being disregarded. Given equal conditions of extent and bulging of the retina, it is much easier to cure a detachment of one or two months' duration with a small rent than one only a few days old with a large tear. The urgency in most cases does not lie in surgical intervention so much as in the need for bandaging the patient's eyes and enforcing relative repose.

Another of the factors which has most influence on the evolution of the retinal detachment and on its cure is the condition of the choroid. During the last few years I have attached considerable importance to this factor. Just as the retina becomes detached because it is altered, so the choroid must be assumed to be changed, in view of the effect which pathologic processes of the one have on the other. However, it has been seen that intense processes do not predispose to detachment because adhesions are created between the two structures. Therefore, not much change in the choroid is required to make a retinal detachment possible. In many cases the ophthalmologist is not aware of the degree of change, and he can enlighten himself about this only by the condition of the fundus and the clinical course of the detachment. A detachment which is replaced with rest has a good prognosis, for the choroid is demonstrated to be in good condition for reabsorption. This proves its relative integrity, a necessary condition for exudation under irritating thermic action and for later reabsorption of the exudate and of the remaining subretinal fluid.

On the other hand, there are cases of recent detachment in which an apparently benign ophthalmoscopic picture is present (small hole and little retinal prominence) but in which there is little, if any, improvement with rest and a severe reaction on surgical intervention occurs.

These cases, which differ from the preceding type, are those in which the choroid has no capacity to reabsorb and in which its probable inflammatory state causes it to respond to surgical attack with a severe local reaction. A similar reaction also appears in the episclera and in the bulbar conjunctiva.

Owing to this variable reactivity of the choroid, which cannot always be predicted, the prognosis of retinal detachment can be only approximate. In some apparently simple cases treatment fails, while in others with extensively detached retinas the outcome is successful because the choroid is healthy and has great absorptive powers.

Likewise, the manner in which the choroid reacts has an influence on the intraocular pressure, aside from the part which the ciliary body itself plays. Some years ago it was believed that very low intraocular pressure was of bad prognostic significance and that normal pressure was a favorable sign. In general, this principle can be accepted, but with many reservations.

If there are large recent tears, the tension is usually low. However much the choroid absorbs, it is not able to absorb all the vitreous which passes behind the retina. After a few months, even though the large rents persist, the tension rises to normal because the choroid cannot absorb more and is undergoing atrophy.

If the holes are small and the tension is reduced, the prognosis is often good, because this indicates choroidal absorption of the subretinal fluid. If the holes are small and the intraocular pressure at the same time remains elevated, the prognosis may be less favorable than would otherwise seem apparent, since this may indicate poor absorptive ability of the choroid.

As already indicated, irritation of the ciliary body may alter these relations, since it is clinical experience that cyclitis may be accompanied with elevated or reduced intraocular pressure.

It is an undoubted fact that the vitreous acts as a foreign body on the choroid, which is finally destroyed. For this reason, all retinal detachments of more than two years' duration are accompanied with complete atrophy of the choroid, as revealed by ophthalmoscopic examination and histologic study. To produce this atrophy, it is logical to assume that the vitreous has acted as an irritant to the choroid. The manner in which the choroid reacts in each case probably varies in different patients, this may be a partial explanation of the various forms of clinical evolution of retinal detachments. To this variable choroidal response to contact with vitreous is added the variable reaction to surgical thermic intervention. Therefore, in the immediate postoperative period, if the eye is not hyperemic, the pupil dilates well and the patient has no pain, the prognosis is much more favorable than if the patient is in pain, the pupil does not dilate with atropine and the eye is hyperemic—all of which are symptoms of uveitis.

Consequently one is forced to the conclusion, already stated so often in part by other authors and by myself, that it is advisable to localize the diathermic action as much as possible. To attain this, a thorough study of the fundus is necessary. To be sure, it is easier and more convenient not to make a detailed study of the fundus by means of direct and indirect ophthalmoscopy, substituting for this procedure lavish use of diathermy over an extensive area. But this convenience is prejudicial to the patient by reducing the chances of a successful result. If it becomes necessary to reoperate, the difficulties are considerably increased in an eye which has undergone excessive diathermic treatment.

Immediate repetition of the operation is advisable only when tears appear which were not reached by the preceding diathermic action. If a second operation is thus indicated, efforts should be made to insure that at least twenty days have elapsed since the first operation, that the eye does not suffer from the pain and photophobia which are characteristic of iridocyclitis and that an exaggerated local reaction is not present. In the cases in which recurrence takes place within the first two months after operation, if no tears are seen or if those which appear are situated in the area treated by diathermy, it is best not to reoperate. It is preferable to apply a binocular bandage and to make the patient rest in bed. The result of the operation may yet be successful. In certain cases with a large bullous retinal pouch, puncture of the site and injection of air into the vitreous may contribute to a cure.

Treatment of retinal detachment gives the highest percentage of successful results if it is based on the following management:

- 1 Thorough exploration of the entire retina by direct and indirect ophthalmoscopy, using a strong illumination with the pupil dilated maximally.

- 2 Repose of the patient with binocular bandage in bed, or almost horizontally in an easy chair, before operation if the retina which surrounds the tear is close to the choroid. If the condition of the eye does not improve after fifteen or twenty days, operation may be undertaken, even though the prognosis is guarded. Although there are cases in which more time is required for the retina to become reattached, it is dangerous to wait longer, because macular vision will be more involved, especially in detachments involving the superior temporal quadrant. It is known that retinal separation in the inferior nasal quadrant is less serious with respect to macular vision and deteriorates more slowly.

- 3 Use of as limited diathermic action as possible, based on accurate localization of the tears, coagulation with weak intensity and as little fulguration as possible. Fulguration burns and irritates the tissues and causes the formation of toxic products, which are irritating to the choroid and prejudicial to a cure. There are patients who do well in spite of the inadeptness of the surgeon, but the percentage of successes is low under such conditions.

4 Ophthalmoscopic control during the operation, transparency of the cornea being maintained by instillation of a very little local anesthetic and by continuous moistening with saline solution. If a retinal bulla is present, it should be punctured with a very fine diathermic needle after surface diathermy of the area under the most sloping part and after injection of sterile air at the level of insertion of one of the rectus muscles in an amount to correspond with the size of the retinal prominence. It is a good sign if the subretinal fluid flows out and then suddenly stops, indicating that the retina or the thick vitreous is thus plugging the hole. The eye then regains its tension, and at the same time the cornea becomes opaque. Sometimes 3 cc, or even 4 cc, of air must be injected.

5 Ocular and general postoperative repose. This must be as complete as possible during the first weeks after operation, with the patient supine in most cases and semisupine in cases of inferior disinsertions and of elderly persons. The position of the head is thought not to be as important as was formerly believed, since in cases in which the patient for one reason or another could not lie on the side of the retinal holes a successful cure was as easily obtained. Perhaps, since the subretinal fluid is denser than the vitreous (as demonstrated by Weve in 1933 and confirmed by others), the position on the side opposite the tears helps the fluid to slip toward the area of intact retina, where healthy choroid can absorb it. This is a hypothesis which only further experience can confirm. In any case, one can be guided by the appearance of photopsias and place the patient on the side in which they are least evident. If photopsia is not present, so much the better, since it is evidence that the retina does not oscillate. The period of almost absolute ocular and general repose varies between ten and thirty days in bed followed by thirty to one hundred days of semirepose, the period depending on the severity of the condition.

6 General tonic treatment of the patient. The presence of general and accompanying focal causes of the ocular lesion should be looked for, but one should lose no time in investigations without keeping the patient at rest with his eyes bandaged.

7 If a relapse takes place during the first weeks, especially when the patient arises from the bed, complete ocular and general repose is resumed unless new holes or preexisting tears which were overlooked are seen outside the zone treated with diathermy. An attempt should be made to limit the diathermic action.

The removal of the patient to his home presents a problem if he lives at a great distance. In good weather transport by airplane is the best method. When this means is not possible, the patient may be carried home by automobile or train, he must not lie in bed or support his shoulders and back on the back of the seat, but his position must be such that his trunk may act as a shock absorber for his head.

## FLUORESCENT COLORS IN TANGENT SCREEN EXAMINATIONS

JACOB B. FELDMAN, M.D.  
AND  
HAROLD J. ABRAHAMSON, Ph.D.  
PHILADELPHIA

THE NUMEROUS devices for the taking of perimetric fields indicate that manufacturers are always endeavoring to devise a machine which will least divert the patient and thus enlist his cooperation in this subjective test.

Perimeters are usually constructed so that the isopter recordings are out of view of the patient, usually at the back of the instrument. This is a distinct advantage so far as the results obtained are concerned. On the other hand, the ophthalmologist does not get the complete picture until the entire field is plotted.

When the tangent screen is used, the recording is clearly seen on the board, and the observer can note very early in the examination at which portion within the 30 degree area there is evidence of scotoma or sector defect. The ophthalmologist can then carefully analyze this location without fatigue to the patient. In the examination of patients with the tangent screen, notations are made by a variety of colored pins or chalks. This array of colors tends to increase the subject's curiosity, and one notes occasional movements of the eye from the point of fixation.

With the colored pins, it is somewhat difficult to take the fields of both eyes at one time. Usually one field is taken, the readings are transferred to the record sheet, the pins are removed, and the procedure is repeated for the other eye. Some tangent screens are made of cloth, so that the pins are easily inserted. The screen is then reversed for the taking of the field of the other eye. This is somewhat less time consuming, though it also inordinately delays the examination. Furthermore, pins often tear the fabric in a cloth tangent screen. After a short period of use we note a "turning" of the free edges of the tangent screen—the inner and outer sides. (The upper and lower parts of the screen are held straight by poles running along their borders.)

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From the clinic of St. Christopher's Hospital for Children

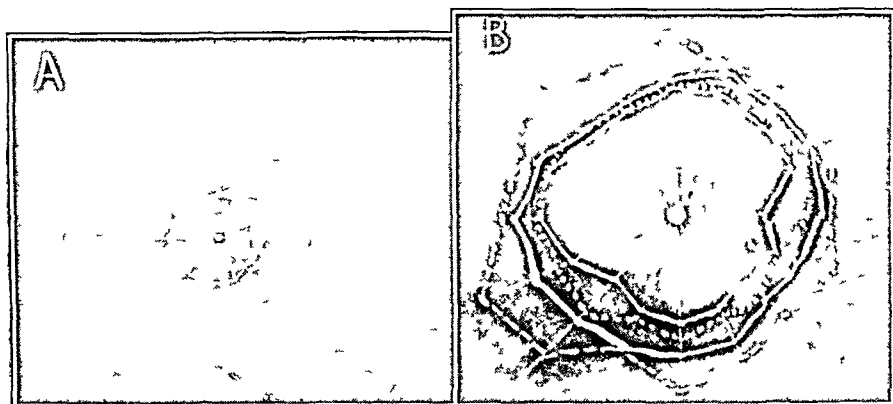
Read at a meeting of the College of Physicians, Philadelphia, Section on Ophthalmology, Feb. 21, 1946

In view of these difficulties, it appeared to us that the speed and efficiency of this examination could be improved. The ordinary black-board or tangent screen now in use could be utilized, but in place of the chalks and pins fluorescent water colors, which can be easily washed off, could be employed in plotting the isopters.

#### METHOD

The technic in taking the field does not vary in any respect from the usual one except that the recordings of the isopters are made by fluorescent colors, almost invisible in white light. These are applied with a fine, inexpensive camel's hair brush glued to an applicator. The pigments are of the water color type,<sup>1</sup> are not dangerous to handle and can be conveniently washed off with either water or soap and water.

The ophthalmologist can readily see the notations on the tangent screen under the usual 7 foot candle illumination used in the test.



In *A*, the screen was exposed to the light for several weeks but did not lose its quality of fluorescence. The pigment cannot be erased except with water. This photograph was taken with the aid of two Photo-Flood lamps, at a distance of 2 meters.

*B* is the same picture taken in absolute darkness with one small, hand type ultraviolet ray lamp. This being a black and white film, one does not see the fields in the actual colors, as portrayed on the tangent screen. This photograph was taken at a distance of 1 meter.

After the study is completed, the ultraviolet light is turned on. Within several minutes the entire field becomes clearly and brilliantly illuminated. The records are now ready for transferral to the history chart.

#### COMMENT

Any tangent screen now in use can be easily converted into the fluorescent type by going over the circles and meridians with fluorescent green pencil. These lines in fluorescent pencil are quite invisible to the patient. As for the ultraviolet ray lamp, almost every hospital

<sup>1</sup> Fluorescent colors can be obtained from Stroblite Co., New York, or Switzer Brothers, Cleveland.

has one for use, in the pathologic, dermatologic or ophthalmologic department

The fluorescent equipment is inexpensive and should last for a number of years

The figure shows photographs of the fields in a case of retinitis pigmentosa plotted on the tangent screen. *A* was taken with fluorescent colors and illuminated with ordinary light. The stimulus used was a 4.5 mm test object at 1,000 mm. Dotted lines are used for the field of the right eye, solid lines, for the field of the left eye. The outer lines are for white stimulus the inner lines, for red stimulus. *B* is the same screen illuminated with ultraviolet light.

#### SUMMARY

A method is shown by which fields can be taken on the tangent screen under regular illumination and plotted with the ordinary targets now in use, but marked off by invisible fluorescent colors read under ultraviolet illumination.

37 South Twentieth Street



## USE OF BERMAN LOCATOR IN REMOVAL OF MAGNETIC INTRAOCULAR FOREIGN BODIES

LOREN P. GUY, M.D.  
NEW YORK

**D**URING the past two years, at the New York Eye and Ear Infirmary, a relatively new instrument, the Berman Locator, has been found increasingly useful for intraocular foreign body work. In fact, experience with this device has demonstrated that the best foreign body work cannot be done without it.

Among a considerable number of cases of intraocular foreign bodies encountered during that period, we have had at least 6 in which the body was at first given up as nonmagnetic because of lack of response to the giant magnetic extractor but was later shown to be magnetic by the Berman Locator and was removed. The initial failures in these cases occurred because roentgenologic localization alone was inadequate to enable the surgeon to apply the proper magnetic power at the correct site to get a response.

In 1 case different surgeons made three attempts to remove the foreign body without getting the slightest response with the giant magnet and concluded that the foreign body was nonmagnetic. Nine months later the Berman Locator, which had not before been available, showed that the foreign body was magnetic, and it was readily localized. However, it was too late to save the eye, for degeneration had already set in. A chart showing two roentgenographic localizations of the foreign body is presented (fig 1), with a photograph of a section of the eye (fig 2). It will be seen that the roentgenograms differed and were thus a source of confusion. The inability to get a response to the giant and hand magnets was obviously due to failure to apply the magnets in the correct location.

These experiences raise the question "What is the Locator and what has it to offer the ophthalmologist that the x-ray machine does not have?" Briefly, the Berman Locator is a portable electromagnetic device similar in size and appearance to a radio, for the detection and localization of metallic foreign bodies, in particular the magnetic metals (iron and steel). It came into prominence in December 1941, when, during the attack on Pearl Harbor by the Japanese, Dr. John J. Moorhead, of New York—for whom the Locator was originally designed by Mr. Samuel Berman, an engineer—demonstrated in the treatment of

casualties of that attack the speed and accuracy with which the Locator would detect and localize magnetic foreign bodies

The Locator gives the surgeon the following practical aids not available to him heretofore

First, and foremost, it is a localizer that he can use himself, if necessary, at any time, in any place and in any emergency

The Locator is self sufficient in many cases for all preoperative and operative localization of magnetic foreign bodies, and when roentgenograms and expert ocular roentgenographic localization are not readily available, the Locator becomes indispensable to the ophthalmic surgeon, for an intraocular foreign body is always an emergency

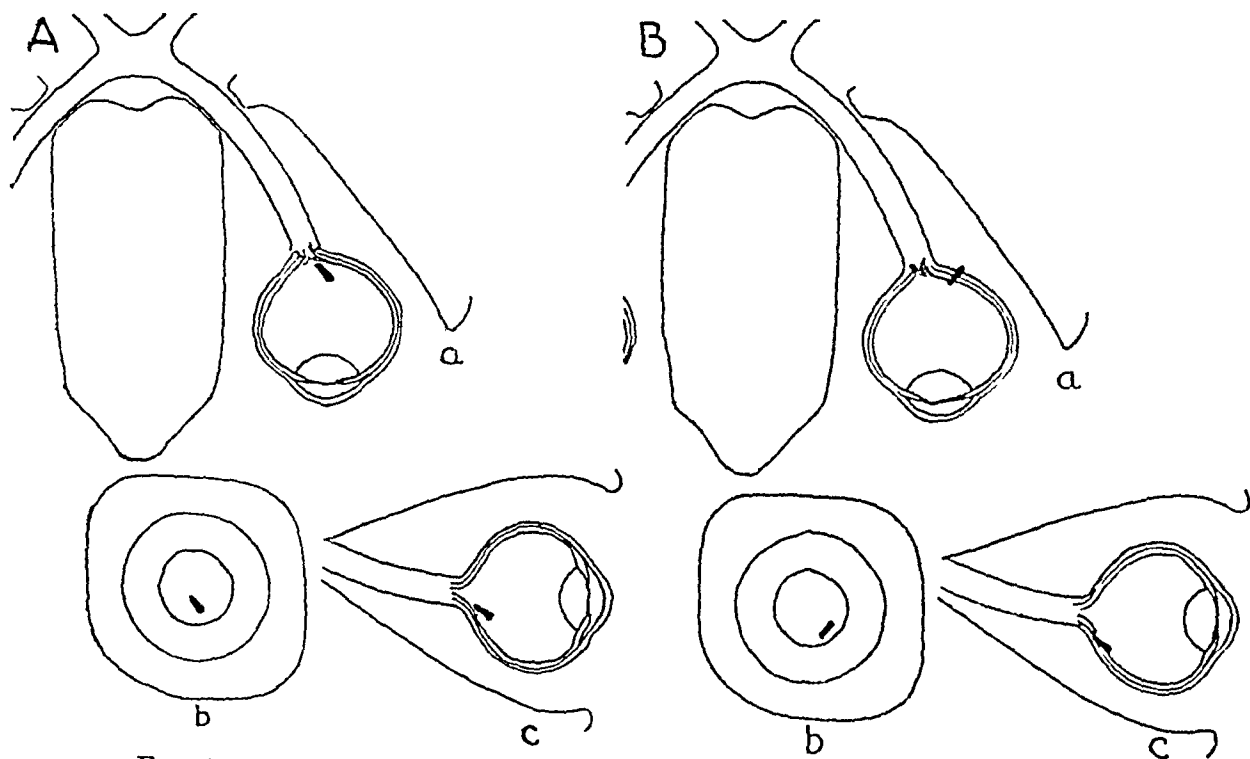


Fig 1—Two roentgenographic localizations of the same foreign body (1.5 by 2.5 mm) in the left eye, scale full size

The data on the position of the foreign body are as follows

(A) Back of center of cornea anterior end, 19.5 mm, posterior end, 21.5 mm  
Horizontal plane anterior end, 3 mm below, posterior end, 2 mm below  
Vertical plane anterior end, 0.5 mm to temporal side, posterior end, 1 mm to nasal side

(B) Back of center of cornea anterior end, 21.5 mm, posterior end, 24 mm  
Horizontal plane anterior end, 4.5 mm below, posterior end, 2.5 mm below  
Vertical plane anterior end, 1.5 mm to temporal side, posterior end, 3 mm to temporal side

In both A and B, a represents a horizontal section, b, a front view, and c, a side view, of the eye

In the operating room, the Locator provides localization of pinpoint accuracy with which to check and, if necessary, to correct the roentgenologic localization previously obtained. If the position of

the foreign body changes, owing to gravity or surgical manipulation, this knowledge is made available instantly

Since intraocular foreign bodies are usually removed by magnetic extraction, it is important to know beforehand whether, and to what degree, the foreign body is magnetic, in order that the proper degree of magnetic force may be used for the extraction. The Locator provides this information, which is valuable, as too much magnetic force causes added injury to the eye and too little is ineffective.



Fig 2—Section of eye, showing actual location of the foreign body indicated in figure 1

The detecting element of the Locator is sufficiently small for practical use in intraocular foreign body work and is sterilizable.

At the New York Eye and Ear Infirmary we have found the operation of the Locator simple and readily mastered by the regular operating room personnel and surgical teams, who have learned to use it successfully, without difficulty.

#### ROENTGENOLOGIC LOCALIZATION AND THE BERMAN LOCATOR

Roentgenograms and roentgenographic localization of intraocular foreign bodies are valuable and often indispensable and, where avail-

able, should not be omitted. They show the presence of most foreign bodies, whether magnetic or not, and they furnish a permanent record that there was a foreign body. They also show its size, shape and general disposition, which constitutes essential preoperative information.

To be of value for the localization of intraocular foreign bodies, however, this type of roentgenologic work must be done by highly skilled specialists who are especially versed in the better technics of ophthalmic roentgenologic localization, such as the Sweet, Vogt or Comberg method. As many communities do not have roentgenologic special-

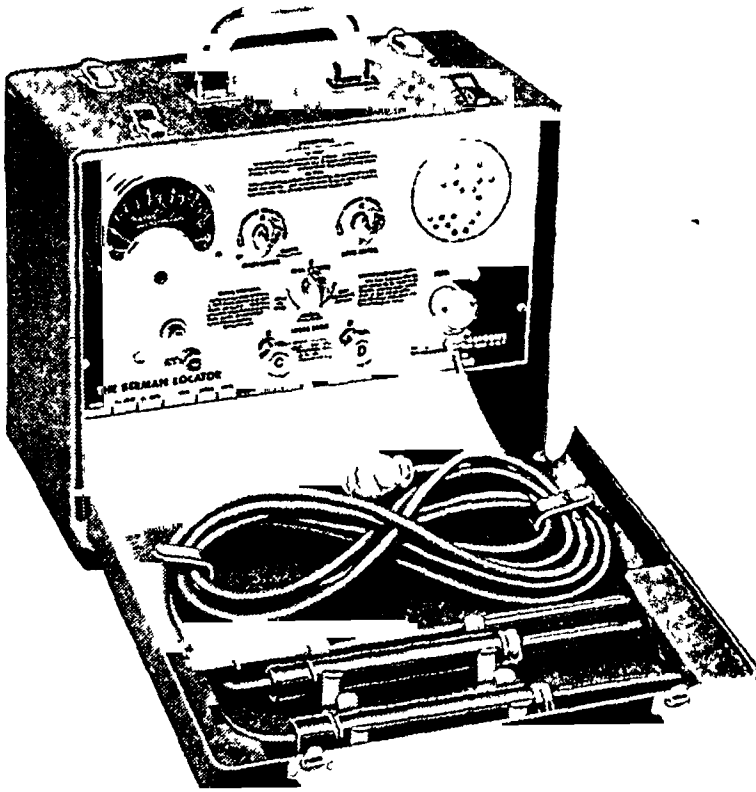


Fig 3—The Berman Locator

ists of this type the electromagnetic localizer fills for them an especial need.

A small percentage of roentgenologic localizations, even by experienced persons, are at times, for one reason or another, sufficiently in error to result in failure to extract the foreign body after the patient reaches the operating room. It is a mistaken notion that an error of 1 or 2 mm is not serious and that the extracting magnet will always cause the fragment to come "from around the cornea" even when the incision is slightly removed from the true site. We have had cases at the New York Eye and Ear Infirmary in which the magnetic extractor was ineffective until a difference of 1 mm, as indicated by the

Locator, was corrected. After the incision was extended 1 mm in the direction indicated, the foreign body came out immediately. Sometimes roentgenograms taken by the same technician and interpreted by the same specialist disagree and cause confusion. In cases such as those cited, the Locator settles the question of localization simply and directly.

Another situation that occasionally, although infrequently, faces the surgeon is a negative roentgenogram despite the existence of a small foreign body. The successful removal of such a foreign body with the aid of the Berman Locator alone was reported recently by Dr. A. R. Sherman, of Newark, N. J.<sup>1</sup>

The combined use of the Locator with roentgenograms meets most of the ideal requirements for localization of foreign bodies. The roentgenogram discloses the presence of the foreign body, its dimensions and general disposition. The Locator tells immediately whether it is magnetic and approximately to what degree. The instrument is then taken into the operating room to be used for checking any previous roentgenographic localizations, which it is capable of doing with absolute accuracy in the hands of the operating room team alone. As the operation proceeds and tissues are disturbed, or if the foreign body has moved, immediate reorientation of the foreign body is available without the necessity of waiting for new roentgenograms to be exposed, developed and interpreted. Localization with the Locator is simple, direct, immediate and precise.

#### OPERATION AND TECHNIC

The operation of the Locator and the adjustment of the controls are relatively simple; at the New York Eye and Ear Infirmary this work is done by the nursing staff. The standard instrument operates on 110 volts alternating current, but models can be built for 110 volts direct current or 6 volt battery operation.

The technic for localizing ordinary intraocular foreign bodies located within or close to the sclera is simple when complete exposure of the surface of the globe at the approximate site is possible.

This involves no more than passing the tip of the sensitive probe over the suspected area and observing the indicating meter or listening to the changing pitch of the built-in loud speaker. As the probe approaches the site of the foreign body, the meter needle rises on the scale, and simultaneously the sound from the speaker rises in pitch. The position on the surface where the peak indication is obtained marks the precise spot for incision.

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1 Personal communication to the author

After the scleral flap is lifted, the tip of the probe may again be applied over the exposed area for reorientation of the precise spot in the choroid for incision. Thus, the operation is characterized by the utmost precision throughout.

The technic is somewhat modified in cases of foreign bodies situated far posteriorly, in which complete exposure of the affected area is difficult and in which there may be a possibility that the foreign body is extraocular and is located within the tissues of the orbit, and not within the globe. While in actual practice the localization in these, more difficult, cases is as rapid as in the simpler cases, a much more intimate knowledge of and familiarity with this technic are required. Besides a study of the technic, some actual practice in the localization and extraction (with forceps) of small foreign bodies buried in a

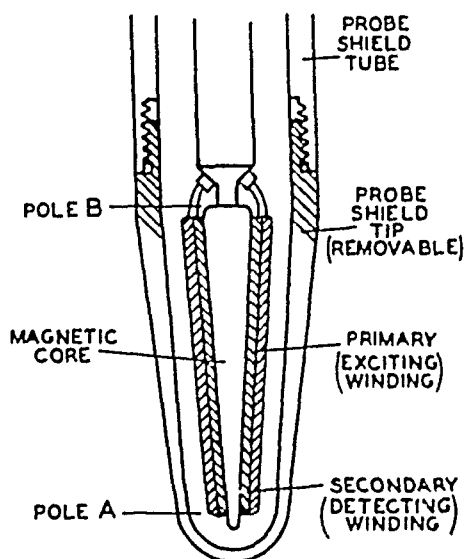


Fig. 4—Construction of the probe of the Berman Locator

suitable medium, such as plastic modeling clay, is essential for complete familiarity with the technic. This normally requires but a few hours and once mastered becomes very simple. To an ophthalmologist who has so many difficult technics to master, this is virtually child's play, nevertheless, the preliminary practice in clay is necessary to make sure that the principles are thoroughly understood and to acquire the degree of skill and familiarity necessary for the operating room.

A description of the principles of the Locator and their application to ophthalmology follows.

#### PROBE

Figure 4 is a diagrammatic section, somewhat exaggerated, of the Locator probe, showing the principal parts. The primary, or exciting winding, creates an alternating magnetic field about the probe and renders its magnetic core a bar magnet having two magnetic poles, *A* and *B*,

as shown. Through the secondary, or detecting winding, the changes in this field caused by the approach of a metallic body register on the indicator. The closer the approach of a metallic body to the probe, the higher the indication. The alternating field about the probe is of low intensity, suitable for the purpose of detection and not for pulling or tractive force.

#### PRELIMINARY EXAMINATION OF A PATIENT

The tip of the probe is first applied to the closed lid. If a ready response is obtained, the search is continued in this manner, the probe being moved along the surface until the surface localization is determined by observing where the peak indication occurs. If no immediate

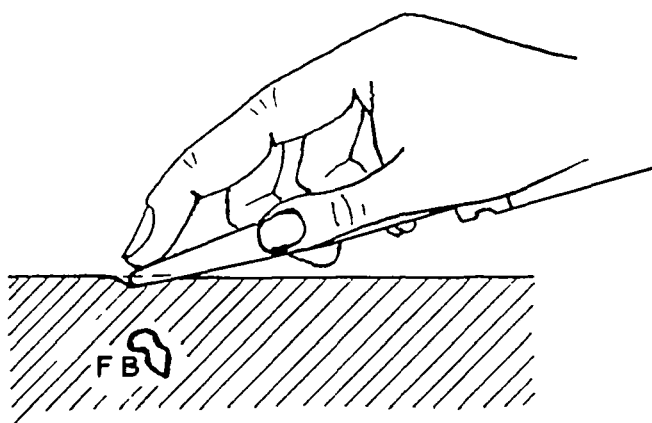


Fig 5—Foreign body barely within range. The probe is pressing into the tissues and pressure relaxed in regular rhythm.

response is obtained, the probe is pressed into the tissues, as shown in figure 5, in order to effect a closer approach to the foreign body.

As shown in the illustration, the probe is not held in the normal manner, by its handle, but is held close to the tip, and the tip is pressed into the tissues directly with the forefinger so as to avoid bending of the tip. This is important, for should the tip bend sufficiently to make contact with the internal sensitive element it might result in a response similar to the approach of metal, leading to what is termed "pressure error." Normally, the outer shield will withstand about 1 pound (453 Gm) of sidewise pressure before deflecting sufficiently to make contact with the internal element. A much greater pressure can be withstood safely head on against the tip.

The probe is pressed in and pressure relaxed in regular rhythm of about 1 second per cycle, if there is a foreign body within range beneath the surface, the indicator response will rise and fall in the same rhythm and in exact synchronism with the motion of the probe. The peak

position is determined by repeating these pressure cycles progressively from point to point along the surface and choosing the point where a maximum response is obtained. If sufficient response is obtainable, a final check is made, in the same manner, with the probe held perpendicular to the surface, for maximum accuracy in localization.

This search must be carefully conducted along the entire orbital rim.

Where a peak indication is obtained, the probe is held against the lid at that point, and the patient is instructed to open his eye and to rotate the eyeball alternately in the several different directions. A consistent change in response with movement of the globe indicates at once that the foreign body is intraocular or is in tissues associated with movements of the eye. If no change in response takes place with rotation of the eyeball, the foreign body is extraocular.

If no response at all is obtained, a magnetic foreign body, if one is known to be present, is beyond range from the surface, and initial exposure must be made with the aid of roentgenologic information alone. In the operating room, after the exposure has been extended sufficiently to bring the probe within range, the probe is used for the final localization, to determine the site for incision.

#### PROCEDURE IN THE OPERATING ROOM

*Sterilization*—Sterilizable rubber jackets of surgical rubber are provided with the instrument to render the probe sterile. These are 16 inches (40 cm) long, are accurately fitted and extend from the tip of the probe to well beyond the handle. The rubber jackets may be sterilized by either boiling or autoclaving and are handled in the same manner as surgeon's gloves. To insure ease of application over the probe, they must be thoroughly dry inside and out. No part of the probe itself is boilable.

*Adjustment of Locator*—The Locator is placed several feet from the operating table, the necessary connections are made, and the controls are turned on and adjusted in accordance with the operating instructions for the instrument. For localization of intraocular bodies the tip portion of the external shield of the probe is unscrewed, so that the smaller diameter of the internal element may be utilized and closer approach to the foreign body made possible. The bare element must always be covered with a rubber jacket, whether sterile conditions are required or not.

It is best to employ an assistant, when available, to handle the Locator and the probe. This avoids the necessity of laying the probe down on the table, from which it may fall and be damaged while the surgeon is otherwise engaged.



*Magnets*—When used, magnets must be at least 6 feet (180 cm) away from the Locator probe. A magnetized probe requires demagnetization in order to be restored to full usefulness. Magnetization of the probe is recognized by sudden reduction in sensitivity and extreme difficulty in tuning the Locator.

*The Operator*—After adjusting the Locator, the operator scrubs and wears a sterile gown and gloves. While an unsterile assistant holds the probe, suspended by its cable, the operator applies a sterile rubber jacket over the probe and grasps it by its handle. The operator may then make his other hand unsterile for the purpose of manipulating the Locator controls and for keeping the unsterile probe cable clear of the field.

*The Operating Table*—An operating table of wood or other non-metallic material is highly desirable. When a metal operating table is used the field must be raised at least 15 inches (38 cm) above the table, using sandbags, pillows or other nonmetallic material. This is particularly important when a foreign body cannot be detected preoperatively from the surface, in which case the necessity for this precaution must not be underestimated. When a strong response is obtained preoperatively and there is no likelihood of fragmentation of the foreign body, so that only low sensitivity will be required in the operation of the Locator, a distance of 8 to 10 inches (20 to 25 cm) from the operating table will suffice.

*Metallic Instruments*—After the preoperative localization has been made, the patient is prepared for the operation. All metallic instruments such as towel clips and hemostats, must be at least 5 inches (12 cm) from the field.

Even the so-called nonmagnetic speculum often has sufficient influence to affect the Locator indications. This can readily be checked before operation. It may be removed from the field while the probe is being used and replaced afterward. Retractors must be non-metallic, boilable lucite is an ideal material, but wooden tongue depressors or traction sutures are satisfactory.

*Surface Localization with Adequate Exposure*—If at all possible, the operative site should be exposed so as to permit the use of the probe perfectly perpendicular to the surface of the eye, as shown in figure 6.

Surface localization under these conditions is simple and accurate. The site for incision is beneath the center of the probe tip, where the "peak" indication is obtained.

*Guarding Against Pressure Errors*—Pressure against the surface must be limited to a minimum, yet contact with the surface must be maintained at all times. For all intraocular work, the probe is

used with the shield of the probe tip removed and the sterilizable rubber jacket covering the bare element. Besides providing protection for the sensitive element, the rubber jacket also serves to provide a smooth, nonabrasive surface for use against the ocular tissues. The probe is grasped near the tip, and the hand is steadied against a nearby surface to facilitate the delicate handling of the probe required for this work (fig 6). With reduced sensitivity of the Locator and with light contact against the surface, there should

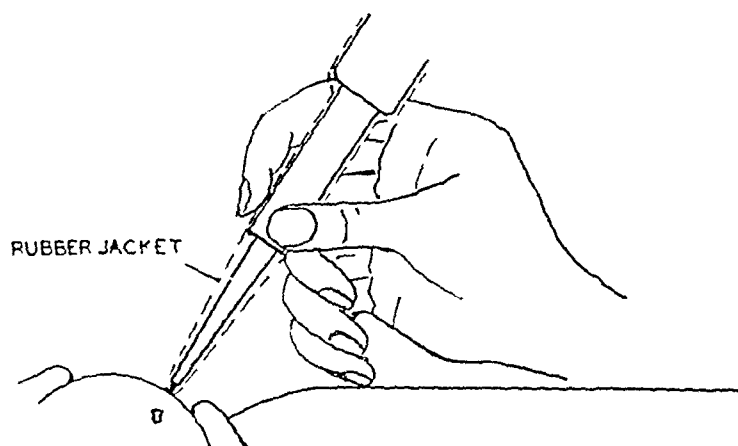


Fig 6—Localization of an intraocular foreign body. The shield of the probe tip is removed, the sterilizable rubber jacket covers the bare element, the probe is grasped near the tip, and the hand is steadied on a nearby surface for delicate handling.

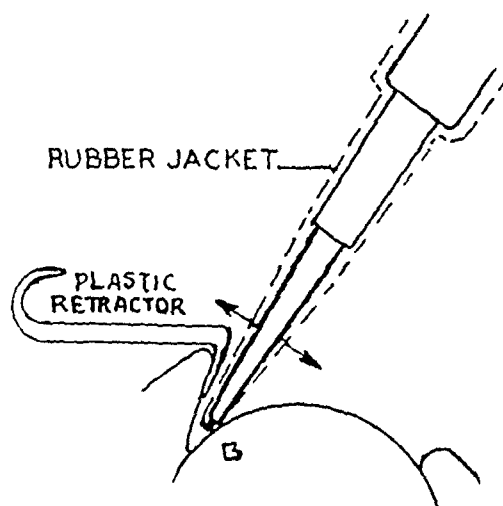


Fig 7—Intraocular foreign body with difficult exposure. The arrows indicate direction of movement of the probe to determine whether the foreign body is intraocular or extraocular.

be no false indications due to pressure only. The operator checks this point at once by applying the probe to the gloved hand with the same degree of contact pressure and the same kind of movement that is required in the localization.

*Localization with Difficult Exposure*—When conditions do not permit complete exposure of the operative site, and localization is required in a partly closed space, as shown in figure 7, the accuracy

is somewhat less than that possible under conditions of complete exposure. With the shield of the probe removed, the peak position is practically opposite the tip of the magnetic core, as shown in figure 6. It should be noted that with the shield of the probe in place the peak position is about 6 mm from the tip.

*Check for Extraocular Foreign Body*—After the surface localization is obtained under the conditions shown in figure 7, the probe is moved several times from the globe toward the orbit and back again, as shown by the arrows in the illustrations. If the foreign body is extraocular, the Locator indication will increase as the probe moves from the globe toward the orbit. On the other hand, if the Locator indication increases each time the probe is moved back toward the globe, the foreign body is intraocular. For this manipulation of the probe in particular retraction must be sufficient to permit the probe some free space for moving back and forth without undue pressure against the tip. To check against possible pressure errors in the indications, the probe should be manipulated in about the same manner against the gloved hand, and if any appreciable response results, localization must be repeated with the pressure faults corrected.

*All-Clear Test*—After a foreign body is extracted, the probe is reapplied to the wound with the instrument set for maximum sensitivity in order to check on whether the wound is clear of all metallic fragments.

#### CONCLUSIONS

1 The Berman Locator has been in use over two years at the New York Eye and Ear Infirmary, where its value has been increasingly appreciated, as it is absolutely accurate in localizing magnetic foreign bodies. It is compact, portable and easy to operate, can be used in the operative field and is always available.

2 It distinguishes between a magnetic and a nonmagnetic foreign body, and it indicates the quality and quantity of magnetism.

3 While it can be used independently of roentgenologic localization, it has greater value when combined with the latter.

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# VASCULAR BASIS OF ALLERGY OF THE EYE AND ITS ADNEXA

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**A**LLERGY of the eye is, of necessity, a subdivision of allergy of the body as a whole. It is also a subdivision of hypersensitivity. Clinically, urticaria, asthma and iritis or any other allergic lesion of the eye are very different, basically, they must have the same pathologic physiology. The clinical symptoms, signs and pathologic manifestations of allergy depend on the structure of the tissue which is the seat of the allergic reaction.

In 1935 Woods<sup>1</sup> presented his monograph on the place of allergy and immunity in ophthalmology. This work deals with experimental studies in general ocular immunology, the relationship of allergy to focal infection, vernal conjunctivitis, trachoma, syphilis and tuberculosis, the antigenic properties and reactions of lens protein and uveal pigment, and the use of nonspecific proteins, autoserums, vaccines and specific serums in therapy. Woods's monograph is an excellent introduction to allergy of the eye from the viewpoint of a bacteriologist and an immunologist.

Woods mentioned that "the term 'allergy' is now generally used to denote any form of hypersensitiveness not falling under the strict definition of anaphylaxis and is essentially a term of convenience." According to the authorities he cited, the anaphylactic shock hormone is either histamine or a histamine-like substance. The union of antigen and antibody, taking place in a few or in many cells, results in cell injury. Since allergy and hypersensitiveness may both be part of anaphylaxis, it is probable that this hypothetical, nonspecific histamine or histamine-like substance is of fundamental importance in any study of allergy.

In 1940 Appelbaum<sup>2</sup> presented a concise article on allergy of the eye. His conclusions were as follows:

Present knowledge of experimental and clinical allergic phenomena of the eye makes it necessary for the ophthalmologist to keep in mind "hypersensitivity" as an etiologic factor in many common ocular conditions. Allergy no longer con-

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Submitted as a candidate's thesis in partial fulfilment of the requirements for membership in the American Ophthalmological Society.

1 Woods, A C. Allergy and Immunity in Ophthalmology, Baltimore, Johns Hopkins Press, 1935.

2 Appelbaum, A. Allergic Phenomena in Ophthalmology, Arch Ophth 24: 803 (Oct) 1940.

cerns the immunologist alone. The practical application of this knowledge, however, is restricted to (1) the therapeutic use of tuberculin in tuberculosis of the eye, (2) the therapeutic use of uveal pigment in sympathetic ophthalmia and (3) desensitization of patients with cataract who are sensitive to lens cortex with lens protein prior to extraction of cataract.

I agree with his statement that "allergy no longer concerns the immunologist alone" but cannot subscribe to his other conclusions.

In 1941 Bab<sup>3</sup> published a paper in which a philosophic attitude toward allergy was presented. Bab noted that "noninflammatory edematous swellings are often characteristic of allergic states," that "an allergic person knows whence the trouble arises" and that "draught is often said by patients to be the cause of an external eye disease." Bab also quoted Boyd concerning the role of histamine in allergy. Boyd<sup>4</sup> said

it is possible that the union of the antigen and antibody acts like an irritant with the liberation of histamine, thus bringing allergic inflammation into line with ordinary inflammation.

Bab also mentioned that "allergic processes are said to be due in greater part to vascular spasms." However, Bab's article deals in the main with the ocular allergies arising from pollens, drugs used externally and foods. Less is said of those forms of allergy not attributable to specific antigen-antibody reactions.

A few months later, in 1941, Bothman<sup>5</sup> published his comprehensive and instructive article on allergy of the eye and its adnexa. This paper deals with reactions to allergins (foods and pollens) and to drugs, chemicals and cosmetics. A consideration of allergy to cold was purposely omitted by him. Bothman stated that in the allergic attack "an antigen-antibody reaction occurs and frees a histamine-like substance which leads to capillary dilatation, increased permeability of vessel walls and an exudation of serum which contains toxic substances. This is the allergic reaction." There are 27 cases in this article illustrative of allergic responses in the conjunctiva, lids, cornea, iris, optic nerve and extraocular muscles, and there is also a discussion of migraine, allergic glaucoma and allergic cataracts.

In 1942 Lemoine<sup>6</sup> published a short article on allergy of the eye in which the role of the endocrine glands in allergy was emphasized. He said

it would seem that the allergic patient has lowered thyroid function, intermittent loss of sodium and water, edema of shock organ tissues, lowered blood

3 Bab, W. *Am J Ophth* **24** 759 (July) 1941.

4 Boyd, W. *A Textbook of Pathology*, ed 2, Philadelphia, Lea & Febiger 1935.

5 Bothman, L. *The 1941 Year Book of the Eye, Ear, Nose and Throat*, Chicago, The Year Book Publishers, Inc., 1941, pp 7-58.

6 Lemoine, A. N. *Allergies in Ophthalmology*, *Arch Ophth* **28** 79 (July) 1942.

pressure, parasympathetic hyperstimulation, a low blood sugar content and an increase of cholesterol, urea and amino acids

He noted that hypofunction of the thyroid gland and the adrienal cortex can account for these changes, while the secretions of the adrienal medulla and the posterior lobe of the pituitary tend to offset these pathologic physicochemical changes

In accordance with the newer concept of allergy, Lemoiné mentioned that histaminase seems to be of benefit in some cases of food allergy. He apparently agreed with Elschmig and Woods that sympathetic ophthalmia is due to hypersensitivity to uveal pigment, and he seemed to favor treatment with tuberculin for ocular lesions attributed to tuberculosis

Most of the aforementioned authors were concerned with the antigen-antibody reactions which give rise to the allergic lesion. Also most of them stated that either histamine or a histamine-like substance is both the result of the antigen-antibody reaction and the direct cause of the allergic lesion

Because histamine is a chemical body of known composition, because it has a profound effect on capillary endothelium and smooth muscle because it is the probable cause of physical allergy in many cases because it occurs in the body and because it is formed in or accumulates in the body under certain well known conditions, it is my belief that a discussion of allergy from the viewpoint of the etiologic importance of histamine or histamine-like bodies would be complementary to the studies of the authors cited thus far in this article

Owing to the long domination of medicine by bacteriology, there is a widespread belief that because certain micro-organisms produce certain diseases with monotonous regularity similar allergic lesions must always have the same cause, whether it be a streptococcus, a focus of infection, a specific antigen or a virus. Allergy, immunology and anaphylaxis have been the special province of bacteriologists for so many years that the average physician in practice is scarcely permitted the right to an opinion about these matters. Dead bacteria or their products have been introduced parenterally in varying amounts into every part of the body. A special esoteric terminology has been developed, which is understood only by the allergists and immunologists. Many of these investigators are not physicians, but they speak authoritatively about clinical lesions despite the fact that most of their work has been limited to experiments on healthy animals

Much valuable work has been done by the bacteriologists and the immunologists in the past, particularly with regard to diseases due to micro-organisms. However, many problems cannot be solved by the bacteriologic immunologic approach, and I think that allergy is one of them. Despite all the remarkable advances which have been claimed for allergy in recent years, it is my opinion that very little of practical value

to ophthalmologists has been discovered. All ophthalmologists can recall many cases of iritis or choroiditis in which all "foci of infection" were investigated, teeth were removed, tonsils were removed, the prostate was massaged, the reactivity to allergens was determined, the diet was changed and, as a final gesture, injections of tuberculin were given for weeks, months or years. In the course of weeks or months the lesion subsided, and the "cure" was attributed to the tuberculin or to the removal of the teeth or tonsils. In other cases no foci of infection were removed, no tuberculin was given and the lesion improved in the course of weeks or months with the time-honored remedies. Finally, there are the cases of iritis, acute retrobulbar neuritis and even death which have occurred after the removal of a tooth, the opening of a sinus or the parenteral introduction into the body of vaccines or antisera for therapeutic or diagnostic purposes. Many such cases have been reported, but many, many more have probably occurred and never been recorded.

The mention of an accident which followed injections of tuberculin is sufficient to indicate the danger inherent in the use of this substance. Muncaster and Allen<sup>7</sup> reported the case of a woman of 31 who had been given 0.00002 mg of tuberculin (purified protein derivative) intradermally by a school physician. As no reaction had occurred forty-eight hours later, she was given 0.005 mg. For the following ten days the patient felt tired and weak. Then pain, redness, tearing and photophobia developed in the left eye, and a few hours later the right eye was similarly involved. When she was first seen by the authors, she was found to have severe bilateral uveitis. She was hospitalized for three weeks and treated at home for nearly six weeks longer before her vision improved to 20/20. As the vitreous cleared, she was seen to have retinal periarteritis. This was the result of a routine tuberculin test in an apparently healthy adult.

Lockhart<sup>8</sup> recently reported the death of a patient following the intravenous injection of 0.12 cc of triple typhoid vaccine. After a rise in temperature and in the pulse and respiration rates, shock developed and the patient died, despite the use of epinephrine and nikethamide. Death was due to coronary thrombosis.

To most physicians allergy means "hypersensitivity" to protein, whether of plant, animal or bacterial origin. Therefore cutaneous tests, desensitization, removal of foci of infection and various types of shock therapy make up the diagnostic and therapeutic approach to allergy.

To me, allergy includes all those aseptic or abacterial lesions in which the basic pathologic process can be reduced to the common denominator

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<sup>7</sup> Muncaster, S. B., and Allen, H. E. Bilateral Uveitis and Retinal Periarteritis as a Focal Reaction to the Tuberculin Test, *Arch Ophthalmol* **21** 509 (March) 1939.

<sup>8</sup> Lockhart, R. J. *Brit J Dermat* **51** 318 (July) 1939.

of either increased capillary permeability or excessive contraction (spasm) of smooth muscle or both. Smooth muscle, of course, includes the smooth muscle in the arterioles, as well as in the bronchioles and the gastrointestinal tract. The concept of allergy and its treatment which I propose to develop must include as etiologic factors all influences—chemical, nervous, humoral or climatic—which can cause either increased capillary permeability or smooth muscle spasm or both. Since, except for the muscles of the iris and the ciliary body, most of the smooth muscle in the eye is found in the walls of the arteries and arterioles, I think that allergy of the eye can be interpreted as a problem in vascular physiology. For this reason, most of this article will deal with physiology and biochemistry and with clinical reports. Little reference will be made to animal experiments. No proof will be offered that the lesions to be discussed are allergic except to point out (1) that the basic pathologic process of the lesions can be interpreted as a manifestation of arteriolar spasm or increased capillary permeability or both, and (2) that it is the opinion of some ophthalmologists that the lesions are due to allergy.

If the concept of allergy had originated in 1930 instead of in 1903, it is not unlikely that recent advances in physiology and biochemistry would have made the approach to the problem entirely different. The years between 1910 and 1930 were characterized by remarkable advances in these two important preclinical sciences. However, bacteriology was a vigorous, rapidly growing branch of medical science long before 1903. Because anaphylaxis (experimental fatal allergy in animals) was associated with the injection of bacterial and other proteins into animals, allergy and anaphylaxis became the special protégés of bacteriology.

If the concepts of allergy and anaphylaxis had not evolved until 1930 or 1935, or if the recent advances in physiology had preceded the development of bacteriology, it is not unlikely that the various manifestations of allergy would have been investigated as problems of physiology rather than of bacteriology. Only ten years ago Horder<sup>9</sup> said

What was disease but a state of morbid physiology? The functions by which a man lived in health were the same as those through which he expressed his pathologic state.

In a recent article, entitled "The Role of the Terrain in the Development of the Polyneuritides," Lecoq and Vignal<sup>10</sup> stated that the constitution of the "terrain" may depend on racial, hereditary or personal antecedents, on temperament, endocrine type, and the neurovegetative and reticuloendothelial systems, on the state of nutrition and metabolism, on pathologic invasion, and on environmental variations. They

<sup>9</sup> Horder. Brit M J 1 632 (March 25) 1935

<sup>10</sup> Lecoq, R., and Vignal, O. Presse méd 48 331-332 (March 27) 1940



cited Olmer's statement that except for trauma, accidental intoxications and acute infection there is really no line of demarcation between the normal and the pathologic and that it is often by imperceptible degrees that disease is instituted. Lecoq and Vignal also stated that in some of the avitaminoses the most important factor is not so much the avitaminosis as it is the humoral disturbance resulting from it.

Moreover, Gajdos,<sup>11</sup> eight years ago stated that histamine could be considered a specific chemical intermediary between the variability of causes and the identity of the reactions of the organism in hyperergic diseases. He expressed the opinion that histamine is the link between cause and effect in certain morbid processes, giving to the pathogenesis a new orientation, which can be compared with the conception of the role of humoral agents in normal physiology, namely, of epinephrine (or sympathin) as a transmitter of sympathetic impulses and of choline (acetylcholine) as a transmitter of parasympathetic excitation.

Likewise, Albus<sup>12</sup> has suggested, on the basis of physiologic and pharmacologic studies, that the more comprehensive term "histamine-susceptible constitution" be substituted for "allergic constitution."

Tooke and Nicholls,<sup>13</sup> in discussing changes in the fundus associated with cardiovascular hypertension, referred to Ricker,<sup>14</sup> who stated in 1927 that the underlying mechanism of both hypertension and inflammatory conditions is a neurovascular defect. Various stimuli cause a constriction of all terminal vascular segments (arterioles). The capillaries become fatigued and relax, as occurs after an overdose of epinephrine. With constricted arterioles and dilated capillaries there is slowing of the blood stream in the capillary bed. The capillaries next become more permeable, as a result either of lack of oxygen or of opening up of spaces in the capillary walls. Depending on the degree of increased capillary permeability, the type of transudate and the degree of slowing of the blood stream, Ricker differentiated three stages: (1) prestasis, or liquor stasis, in which plasma (and fibrin) are found in the transudate, (2) peristasis, or leukostasis, in which white cells (chiefly lymphocytes) also pass into the perivascular tissues, and (3) stasis, or rubrostasis, in which erythrocytes pass through the capillary walls. Krogh confirmed Ricker's observations. In their simplest forms, it must be apparent that prestasis causes urticarial lesions, peristasis produces lesions characterized by perivascular edema and round cell infiltration and stasis results in purpuric lesions. Lesions attributed to allergy, focal infection, histamine poisoning or overdoses of epinephrine and even

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11 Gajdos, A. *Presse med* **46** 509 (April 2) 1938.

12 Albus, G. *Ztschr f d ges exper Med* **108** 592 (March 3) 1941.

13 Tooke, F. I., and Nicholls, J. *Am J Ophth* **21** 395 (April) 1938.

14 Ricker, G. *Sklerose und Hypertonie der innervierten Arterien*, Berlin, Julius Springer, 1927.

the lesions of B avitaminosis can be interpreted as due to varying degrees of prestasis, peristasis and stasis

In my opinion, all abacterial lesions designated as manifestations of allergy show varying degrees of prestasis, peristasis and stasis. Moreover, all chemical, nervous or other agents which can cause either arteriolar spasms or increased capillary permeability or both must be regarded as direct or contributing causes of allergy

Finally, it must be obvious that the only difference between the normal and the allergic person is one of degree. Every one probably has minor or transitory allergic manifestations during life. Allergic patients have more severe and more frequent attacks of allergy. Fundamentally, the differences between the normal and the allergic person are quantitative rather than qualitative

#### CURRENT CONCEPTS OF ALLERGY AND ANAPHYLAXIS

*Bacterial and Immunologic Aspects*—According to the Seegals,<sup>15</sup> allergy is a condition of hypersensitiveness in human beings. It defines a group of biologic responses in which body tissues have been so altered by previous contact with an antigen that their subsequent reactions to the same inciting agent may be entirely different from those produced by the initial contact. Among the allergic symptom complexes are serum disease and serum accidents, hay fever and asthma, gastrointestinal allergy, skin allergy, drug allergy, physical allergy and bacterial allergy

It is obvious that if allergies due to drugs and physical agents are to be included in the phenomena of hypersensitiveness the Seegals' definition should be broadened by eliminating all reference to antigen. Their definition is too limited because it focuses undue attention on antigen-antibody reactions

Beatrice Seegal<sup>16</sup> noted that anaphylaxis is a type of hypersensitivity in animals experimentally produced by the repeated parenteral injection of foreign proteins. For the purposes of this article, I think it may be assumed that allergy and anaphylaxis are fundamentally the same, differing only in degree. Allergy usually disables the patients, anaphylactic shock usually kills the experimental animal

There are two theories of anaphylaxis, the physical and the chemical. According to the physical theory, the union of antigen and antibody disturbs the colloidal equilibrium of the plasma or the cell protoplasm, which, in turn, so interferes with normal physiologic activity that anaphylactic shock results. According to the chemical theory, a "toxic" substance (anaphylactotoxin) is produced by the union of antigen and

<sup>15</sup> Seegal, D, and Seegal, B. C., in Gay, F. P. *Agents of Disease and Host Resistance*, Springfield, Ill., Charles C Thomas, Publisher, 1935, pp. 79-112

<sup>16</sup> Seegal, B. C., in Gay, F. P. *Agents of Disease and Host Resistance*, Springfield, Ill., Charles C Thomas, Publisher, 1935, pp. 36-78

antibody There are many variations of this theory, and many workers think that this toxic substance is liberated not from the injected antibody but from the animal's own antibodies, plasma or tissues One school believes that this "anaphylactotoxin" is either histamine (Dale) or a histamine-like substance (Lewis)

Topley<sup>17</sup> discussed the histamine origin of hypersensitivity clearly and logically After mentioning that the symptoms and lesions of anaphylactic shock are constant for a given animal species, irrespective of the nature of the sensitizing antigen, and that they differ sharply from one species to another, he stated

Histamine is a relatively simple substance of known chemical constitution It can hardly be a mere coincidence that on intravenous injection it mimics so closely the syndrome produced by the injection of a nontoxic antigen into a sensitized animal

After noting that the tissues that play the most dramatic part in anaphylactic shock are exactly those that are sensitive to histamine, he continued as follows

Whether the cells that are injured and liberate histamine are themselves histamine-sensitive, whether minimal injury may so disturb the internal economy of cells that it becomes reactive to its own contained histamine, or whether we should locate the injury and liberation of histamine in one type of cell, the response to the liberated histamine in another, are problems which are not soluble at the moment

He then pointed out that anaphylactoid reactions resemble anaphylactic reactions in that the secondary, histamine-like effect is the same An anaphylactic or anaphylactoid reaction consists, he stated,

of a description of cellular injury, differing from case to case according to the reagent employed and the susceptibilities of the experimental animal, and a histamine effect, differing from one animal species to another according to the distribution of the histamine-sensitive cells but common to all reactions in one animal species by whatever reagents they are caused

In his summary, he stressed the point that the most dramatic features of anaphylactic shock are the result not of the antigen-antibody reaction itself but of the liberation of histamine by the injured cells and the secondary response of the histamine-sensitive cells throughout the body

Findlay<sup>18</sup> also showed that subcutaneous injections of histamine caused the localization of pathogenic bacteria and filtrable viruses (which were injected intravenously) at the site of the injections of histamine He attributed this localization to capillary dilatation and increased capil-

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17 Topley, W W C An Outline of Immunity, Baltimore, William Wood & Company, 1933, pp 192-223

18 Findlay, G M J Path & Bact **31** 633 (Oct) 1928

lary permeability Topley<sup>19</sup> also noted that a diminished oxygen supply to tissues allowed organisms to grow better This suggests that bacterial invasion of tissues may be secondary to circulatory impairment, especially when relatively nonvirulent micro-organisms are the invaders

Beatrice Seegal<sup>16</sup> noted Drinker and Bronfenner's report that amyl nitrite relieved anaphylactic shock in the rabbit She also mentioned that rats are refractory to anaphylaxis and must be kept on a diet deficient in vitamin B before shock can be induced Rats can be sensitized if the adrenal glands are removed Thyroidectomized guinea pigs cannot be actively sensitized She further noted that all the pathologic and physiologic manifestations of anaphylactic shock may be referred to contraction of smooth muscles and increased capillary permeability It is of some interest that in 1914 Mautner and Pick,<sup>20</sup> in treating anaphylactic shock, obtained good results from the vasodilating action of nitrites This agrees with the work of Drinker and Bronfenner In both observations therapy was directed toward smooth muscle spasm rather than desensitization

*Physiologic Aspects*—Evans<sup>21</sup> stated that Dale and his co-workers have reported that in the cat histamine causes arteriolar constriction, capillary dilatation, increased capillary permeability, edema and hemoconcentration Plasma, white cells and even red cells pass out into the tissues Capillary tonus is better maintained, however, in the presence of well oxygenated blood containing minute amounts of epinephrine According to Landis,<sup>22</sup> lack of oxygen in the circulating blood causes the same capillary changes

In 1910, and again in 1919, Dale and Laird<sup>23</sup> commented on the similarity between histamine shock and anaphylactic shock In 1929 Dale<sup>24</sup> concluded that the intracellular antigen-antibody reaction causes intracellular injury which liberates histamine and other substances These "other substances" may account for the signs which are observed in anaphylactic, but not in histamine, shock

In 1931 Best and McHenry<sup>25</sup> reviewed the physiologic aspects of histamine in an article based on over 400 original references They mentioned that histamine can be obtained from nearly all the tissues

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<sup>19</sup> Topley,<sup>17</sup> pages 248-249

<sup>20</sup> Mautner and Pick, cited by Sollmann, T A Manual of Pharmacology, ed 2, Philadelphia, W B Saunders Co, 1922, p 446

<sup>21</sup> Evans, C L Recent Advances in Physiology, ed 4, Philadelphia, P Blakiston's Son & Co, 1930

<sup>22</sup> Landis, E M Physiol Rev **14** 404 (July) 1934

<sup>23</sup> Dale, H H, and Laird, P P Histamine Shock, J Physiol **52** 355, 1918-1919

<sup>24</sup> Dale, H H Lancet **1** 1179 (June 8), 1233 (June 15), 1285 (June 22) 1929

<sup>25</sup> Best, C H, and McHenry, E W Physiol Rev **11** 371 (Oct) 1931

of the body (skin, intestinal mucosa, intestinal contents, white blood cells, feces, muscle, lung, liver, spleen, brain and nervous tissue) It is probably the substance of Lewis, and it is set free by antidromic nerve impulses, axon reflexes and trauma Certain gram-negative bacteria produce it from histidine by decarboxylation It is produced in the skin as a result of exposure to cold air or cold water and also by ultraviolet irradiation While histamine may be fatal if given intravenously in even small amounts, the body apparently can neutralize it, since large quantities may be formed in or introduced into the intestine without causing symptoms Its removal is probably oxidative, either directly or through the mediation of histaminase Oxygen accelerates the histamine-histaminase reaction, and oxygen seems to be a physiologic antidote for histamine

For the guinea pig, which is most susceptible to anaphylactic shock, the approximate minimal lethal dose is about 0.3 mg of histamine per kilogram of body weight, for the white rat, which is almost immune to anaphylactic shock, the minimal lethal dose is 300 mg per kilogram of body weight This last fact supports indirectly the theory that anaphylactic shock and histamine are closely related

Moon<sup>26</sup> notes that in 1911-1912 Dale and Laidlaw<sup>27</sup> stated the belief that the action of histamine typifies the effects of a large class of substances These include bacteria and their products, extracts of various tissues, foreign serums and other proteins, and peptones and other products of protein cleavage All these apparently unrelated substances have one feature in common They injure the capillary endothelium

Moon also noted<sup>26</sup>

suitably large doses of adrenaline [epinephrine] will produce a condition of circulatory failure indistinguishable from shock Adrenalin may produce maximal arterial constriction of such degree that the tissues suffer from anoxia If the lack of oxygen is of sufficient duration and degree, atony of the capillaries and venules will develop in the areas affected

He also mentioned that Cannon had endorsed this as the probable explanation of circulatory failure following injections of epinephrine and had suggested that overactivity of the sympathoadrenal system is a factor resulting from pain, strong emotions and other conditions

From the preceding paragraph it must be apparent that epinephrine which in small doses is a physiologic antagonist of histamine, in large doses is a synergist, since the two substances cause the same arteriolar

26 Moon, V Shock and Related Capillary Phenomena, New York, Oxford University Press, 1938

27 Dale, H. H., and Laidlaw, P. P. J. Physiol. **41** 318, 1910-1911, **43** 182, 1911-1912

and capillary changes. This fact may explain why allergic patients become "epinephrine fast."

Moon, of course, referred to a general shocklike condition which resulted from intravenous injection of epinephrine. In 1940 Cohen and Waterstone<sup>28</sup> noted that local changes occurred in the skin after injections of epinephrine. They reported the cases of 2 Negro women with asthma in whom an area of edema developed at the site of intradermal and subcutaneous injections of epinephrine, followed by local tissue necrosis. These authors compared the lesions to the Arthus phenomenon. From their description, the lesions also resembled a strongly positive tuberculin reaction. They attributed the lesions to anaphylaxis. Obviously, they can be attributed to physiologic reactions which were pathologic in degree.

It may be recalled that Gajdos<sup>11</sup> stated that histamine was the link between cause and effect in certain allergic processes.

Corelli<sup>29</sup> reported that the subcutaneous injection of 0.8 or 1.0 mg of histamine in 14 cases of erythema nodosum attributed to rheumatic fever or tuberculosis intensified the preexisting lesions and caused the appearance of new lesions. Moreover, it intensified positive reactions to subcutaneous and intradermal tuberculin tests. Possibly the tuberculin test is really a test for hypersensitivity to histamine!

It should also be pointed out that histamine is effective in minute amounts. Pickering<sup>30</sup> produced headache by injecting 0.1 mg intravenously, and Maijala<sup>31</sup> reported a case in which the patient died after receiving 0.8 mg subcutaneously. Moreover, Peters and Van Slyke<sup>32</sup> said

Dale, Abel and their associates have shown that it [histamine] is not only highly toxic, but that it has, in minute amounts, such effects on blood pressure, on the contractibility of smooth muscle and on capillaries that it may perhaps, be classed with the hormones.

In 1941, Urbach, Herrman and Gottlieb<sup>33</sup> discussed hypersensitivity to cold, noting that this may be due to an effect of histamine. They stated

under given pathologic conditions the tissue's own protein can undergo alteration, and under the influence of physical agents this altered protein produces

28 Cohen, A. E., and Waterstone, M. L. *J. Allergy* **11** 393 (May) 1940.

29 Corelli, F. *Polislinico (sez med)* **44** 491 (Oct 1) 1937.

30 Pickering, G. W., and Hess, W. *Brit. M. J.* **2** 1097 (Dec 17) 1932.

31 Maijala, P. *Nord. med. tidskr.* **16**:1287 (Aug 13) 1938.

32 Peters, J. P., and Van Slyke, D. D. *Quantitative Clinical Chemistry*, Baltimore, Williams & Wilkins Company, 1931, vol. 1, p. 398.

33 Urbach, E., Herrman, M. F., and Gottlieb, E. M. *Cold Allergy and Cold Pathergy*, *Arch. Dermat. & Syph.* **43** 366 (Feb) 1941.

a histamine-like substance which elicits, for instance, cutaneous manifestations Under the heading of cold pathergy, they stated

Predisposing factors, such as previous infections and other diseases, can bring about a certain degree of instability in the peripheral neurovascular system Physical agents are thus enabled locally to elicit abnormal neurovascular reactions

They also state that "not in every case of hypersensitiveness is the condition to be considered as allergic, i e, based on antigen-antibody reaction "

Later in the same year Harkavy<sup>34</sup> emphasized the role of the blood vessels in bronchial asthma with these words

Since, therefore, the blood vessels appear to be the primary site of the allergic reaction, it may be reasoned that any organ in the body may become a shock tissue if the blood vessels supplying it have become sensitized

In some of his cases, in addition to the pulmonary lesions, there appeared hyperergic vascular lesions in the skin, such as hemorrhagic necrosis (1 case), purpura, urticaria and angioneurotic edema (4 cases) and periarteritis nodosa (1 case) After mentioning the property of histamine-like substances in initiating smooth muscle spasms and increased capillary permeability, he stated that the hemopoietic tissues also participated in the generalized allergic response and that "the bone marrow may therefore be regarded as a shock organ which may react under allergenic stimulation by multiplication of its cellular elements or by suppression" (In other words, agranulocytosis, leukopenia, leukocytosis, eosinophilia and even leukemia may all be due to the same type of stimulus, but quantitative variations in the stimulus and the response of the bone marrow account for marked variations in the hemogram (W F D )

Harkavy concluded that not only the bronchi but the myocardium, serous membranes, joints, skin and nervous and hemopoietic systems may be involved in the more generalized vascular reactions and that distinct syndromes may arise which may be reversible or irreversible He expressed the belief that the various lesions in his cases represented hyperergic vascular responses

All the available evidence indicates that allergy resembles a localized manifestation of histamine poisoning Tiny amounts of histamine may be of physiologic importance in regulating capillary permeability In large amounts histamine acts as a "toxin" by increasing capillary permeability beyond physiologic limits It causes tissue anoxia Lack of oxygen can cause the same type of lesions Oxygen is a physiologic antagonist of histamine All agents which can cause increased capillary permeability and tissue anoxia may be concerned in the production of allergic lesions As Moon<sup>26</sup> has said " many phenomena called

34 Harkavy, J Vascular Allergy, Arch Int Med 67 709 (April) 1941

toxic are essentially anoxic" Allergy must be included among these phenomena

It is not unreasonable to assume that any factors which would tend to relieve capillary and tissue anoxia should be of value in the treatment of allergy

#### FOCAL INFECTION AND ALLERGY

It is impossible to discuss allergy without mentioning focal infection because of the belief of many allergists that the subject becomes sensitized to bacterial products which are formed in the focus and later transported by the blood stream to other parts of the body. Countless experiments have been done on healthy animals to prove that ocular lesions are due to distant "foci of infection" and that "elective localization" is a fact, rather than just a hypothesis. It is true that removal of foci of infection is sometimes followed by subsidence of an ocular lesion. It is also true that in many instances the ocular lesion is not affected by such an operation, and in a few instances the removal of a tooth or the "cleaning out" of a sinus is followed by the development of an ocular lesion which the operation is supposed to cure.

With regard to surgical procedures on the sinuses for acute retrobulbar neuritis, Benedict<sup>35</sup> reported that operations on normal sinuses were fully as effective as operations on diseased sinuses. He concluded that this therapy was nonspecific and that improvement could be attributed to the hyperemia resulting from the trauma and the absorption of blood. In other words, the operation acts by means of autohemotherapy and is similar to foreign protein therapy.

Schmidt<sup>36</sup> came to the same conclusion regarding the removal of infected dental roots for chronic iridocyclitis and other conditions. He broached the question as to whether or not the loss of blood, its absorption and the necrosis of tissue following dental treatment might be the equivalent of nonspecific parenteral foreign protein therapy.

Charlin<sup>37</sup> pointed out that ocular lesions attributed to dental infection contained no germs.

Lagrange and Goulesque<sup>38</sup> expressed the opinion that foci of infection in the teeth and sinuses act reflexly by causing antidromic impulses via the sensory fibers of the fifth nerve, either by axon reflexes or by overaction of the sympathetic nervous system, to cause ocular lesions. However, they asserted that hematogenous transfer of the exciting agent can explain lesions of the eyes due either to near or to distant primary

<sup>35</sup> Benedict, W. L. Retrobulbar Neuritis and Disease of the Nasal Accessory Sinuses, *Arch. Ophth.* **9**:893 (June) 1933.

<sup>36</sup> Schmidt, K. *Klin. Monatsbl. f. Augenh.* **93**:191 (July) 1934, abstracted, *Arch. Ophth.* **13**:887 (May) 1935.

<sup>37</sup> Charlin, C. C. *Arch. de oftal. de Buenos Aires* **11**:251 (May) 1936.

<sup>38</sup> Lagrange, H., and Goulesque, J. *Ann. d'ocul.* **175**:493 (July) 1938.



foci of infection Their 3 patients with iridocyclitis improved only after operation on the sinuses Two of their patients were receiving antisyphilitic treatment at the same time Their patients probably improved for the reasons suggested by Benedict and by Schmidt as to the modus operandi of removal of foci of infection

In 1918 Evans<sup>39</sup> stated

[in cases of iritis, iridocyclitis, choroiditis, retinitis, retrobulbar neuritis and postoperative iridocyclitis] no organisms have been found in the blood or in the [anterior] chamber in these cases and truth to tell we have not yet been able to prove conclusively their bacterial origin

In 1933 Evans,<sup>40</sup> after pointing out the defects in the theory of focal infection, suggested

(a) Secondary lesions result primarily from "lowered vitality or resistance" of the tissues secondarily affected (b) Lowered vitality is due to defect of "trophic influence" or to reflex antidromic impulses Antidromic impulses appear to dislocate vascular reflexes and cellular activity (c) The vascular reflex is an essential factor in the maintenance of sympathetic balance, though probably other undetermined factors are also concerned (d) The vascular state of the tissues can be influenced through short and long axon-reflexes The short axon-reflex is salutary and protective The long axon-reflex, antidromic and noxious, accounts for the incidence of the secondary lesion on the same side as the primary lesion

There is much truth in the conclusion of Evans, and he deserves credit for trying to explain the lesions attributed to focal infection as manifestations of disordered physiology, rather than confusing the issue with ultrascientific, but clinically obscure, words and phrases Since antidromic impulses liberate histamine, it will become apparent that his approach and my approach to this subject of allergy have much in common

It has been said that the teeth, tonsils and sinuses are the favorite points of operative attack because they are readily accessible The lower part of the gastrointestinal tract is loaded with micro-organisms of the colon group of bacilli (which are known to produce histamine) Certainly, this region of the body must be considered in any theory of focal infection A praiseworthy note of caution with regard to operations on "foci of infection" was recently sounded by Reimann and Havens<sup>41</sup> After a comprehensive survey of the literature, these authors stated

in the light of present knowledge, the removal of such local infections in the hope of influencing remote or general symptoms and disease must still be regarded as an experimental procedure not devoid of hazard

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39 Evans, J J Birmingham M Rev 83 1 (Jan-Feb) 1918

40 Evans, J J Birmingham M Rev 8 252 (Dec) 1933

41 Reimann, H A, and Havens, W P Focal Infection and Systemic Disease A Critical Appraisal, J A M A 114 1 (Jan 6) 1940

## "SHOCK" THERAPY OF ALLERGIC DISEASES

As mentioned in the preceding section, operations on foci of infection can be interpreted as equivalent to nonspecific parenteral foreign protein therapy or to autohemotherapy. For many years intravenous injections of typhoid vaccine and intramuscular injections of boiled milk have been the favorite weapons for combating allergic inflammations of the uveal tract, optic nerve and cornea. As a modification of this therapy, diphtheria antitoxin is used in treatment of sympathetic ophthalmia, and vaccines other than typhoid are given subcutaneously for a host of conditions.

Except for the fact that the patient knows something is being done to him, it is still a question in my mind as to the real value of these procedures. Moreover, they are not devoid of danger, and when used for extraocular lesions they have been known to produce the type of lesions which they are supposed to cure. Furthermore, death has occasionally occurred after any one of the types of shock therapy for ocular, as well as extraocular, lesions.

Ten years ago Irons<sup>42</sup> collected 140 instances of harmful results, including a number of cases of death, following subcutaneous injection of vaccines. In 17 cases asthma occurred in persons not previously known to have suffered from the condition. Irons noted that Benedict and Rucker reported that foreign protein therapy seemed to be most effective with patients seen early in a first attack of iritis rather than with patients whose disease had been active for several months or patients who had suffered from previous attacks. As Irons said<sup>42</sup>

there is noted a group of favorable cases in which from the natural history of the disease improvement would be most likely to be expected.

Furthermore, in discussing arthritis, both atrophic and hypertrophic, which has been compared with iritis and scleritis by many ophthalmologists, Irons said<sup>42</sup>

While infection is believed by some to be one of the chief factors responsible for the former of these two [atrophic type], in both groups other factors including heredity, poor nutrition, metabolic disturbances [and] impaired local blood supply to mention but a few, play a large part in the production of joint disease and disability.

In an earlier section of this article, reference was made to Lockhart's<sup>8</sup> case, in which death followed intravenous injection of triple typhoid vaccine and to Muncaster and Allen's<sup>7</sup> case, in which bilateral uveitis and periarteritis developed after routine tuberculin test. Sédan and Koutseff<sup>43</sup> reported an allergic reaction of the iris following urethral dilation in a man of 56 who had a chronic periurethral infection and who had previously had several attacks of acute iritis. I can recall 2

<sup>42</sup> Irons, E. E. *Bull. New York Acad. Med.* 7:412 (June) 1931.

<sup>43</sup> Sédan, J., and Koutseff, A. *Ocular Allergy. New Observations*, *Arch. Ophth.* 22:924 (Nov.) 1939.

similar cases, as well as a case in which acute iritis developed in less than forty-eight hours after removal of an "infected" tooth

Brown<sup>44</sup> mentioned that 20 per cent of 75 patients with diphtheria who had received diphtheria antitoxin had papilledema and 10 per cent complained of "blurriness" of vision. He ascribed the lesions to vascular dysfunction.

Theodore and Lewson<sup>45</sup> reported the case of bilateral fibrinous iritis which developed as an accompaniment of serum sickness twenty-two days after the patient had received 80,000 units of type I anti-pneumococcus serum intravenously. The patient also had had serum sickness nine days after receiving the serum. These authors mentioned Brown's report, Mason's report, in which 3 patients had optic neuritis after receiving antiserums, and Bedell's case, in which bilateral retinal edema with hemorrhages developed after an injection of tetanus antitoxin. Theodore and Lewson's patient did not respond to administration of ephedrine by mouth and instillations of epinephrine in the eyes, but he did respond rapidly to atropine and hot compresses.

Similar reactions to vaccines, antiserums and injections of foreign protein, both ocular and extrabucular, have been reported so often that a monograph could be written on this phase of the subject alone. All are probably manifestations of vascular dysfunction, due to varying degrees of arteriolar spasm and increased capillary permeability, with resulting tissue anoxia.

Moon<sup>26</sup> stated that severe reactions following foreign protein therapy are probably due to arteriolar constriction, followed by arteriolar relaxation. Insulin, metrazol and other types of convulsive therapy probably act similarly, but it is not the arteriolar constriction but the succeeding arteriolar dilatation (which occurs just this side of death) which is responsible for the beneficial results in the treatment of nervous and mental diseases reported by many authors.

Even heat therapy, which is fashionable at the moment, and which is basically similar to foreign protein therapy and probably fully as dangerous, is used at times in treating allergic ocular lesions. Histamine may be the culprit here. Many workers have postulated that histamine is the cause of shock following severe burns. Hildebrandt<sup>46</sup> recently reported that both diathermy and short wave therapy increased the histamine content of the blood by several hundred per cent in animal experiments.

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44 Brown, A. L. *Am J Ophth* 8 614 (Aug.) 1925

45 Theodore, F. H., and Lewson, A. C. Bilateral Iritis Complicating Serum Sickness, *Arch Ophth* 21 828 (May) 1939

46 Hildebrandt, F. The Pharmacology of Short Waves, *J A M A* 112 1274 (April 1) 1939

Warren, Carpenter and Boak<sup>47</sup> reported that herpes developed in 46.2 per cent of 411 patients given 545 treatments with fever artificially induced by physical methods. In 3 of the patients herpetic lesions of the cornea, and in 2 congestion of the sclera, developed. Fifteen of the group with herpes showed mild symptoms of meningoencephalitis, and 8 patients without herpes had symptoms of meningoencephalitis. In 2 patients (not in this series) delusional states developed, 1 required restraints for two days. These authors attributed the herpes to a virus! Why not histamine?

Ebaugh, Barnacle and Ewalt<sup>48</sup> reported that there were 399 delirious reactions in 350 patients who had received 2,585 treatments in the Kettering Hypertherm. The average duration of the reactions was about one hour. Ten patients had severe reactions. The authors concluded that "fever exaggerates the subject's outstanding personality characteristics."

Suppose that heating the tissues does produce an increase in histamine, and suppose it does cause "mental episodes" to occur. Is there any evidence that "mental episodes" which are not due to artificial fever therapy are produced by histamine? The literature supplies some evidence.

As early as 1933 Watt<sup>49</sup> suggested that histamine toxemia (probably of intestinal origin) was the cause of severe mental depression.

In 1934 Davidson<sup>50</sup> discussed acute death in 22 "excited" patients with mental disease, death was attributed to "exhaustion." Various organs, including the central nervous system, showed edema and congestion. He attributed the lesions to "capillary toxicosis," endogenous in origin, and concluded "we may perhaps identify them [the toxic substances] with the H-substance of Lewis."

Shulack<sup>51</sup> confirmed the observation that cerebral congestion was the presenting pathologic feature in these cases, and in an editorial in the *British Medical Journal*<sup>52</sup> it was stated that Jahn and Greving had noticed a similarity between these pathologic changes and histamine poisoning in animals.

Collins<sup>53</sup> reported the case of a patient with mild disseminated sclerosis who became paralyzed in all four limbs and anesthetic over

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47 Warren, S. L., Carpenter, C. M., and Boak, R. A. *J. Exper. Med.* **71** 155 (Feb.) 1940.

48 Ebaugh, F. G., Barnacle, C. H., and Ewalt, J. R. *Psychiatric Aspects of Artificial Fever Therapy*, *Arch. Neurol. & Psychiat.* **39** 1203 (June) 1938.

49 Watt, J. C. *Brit. M. J.* **1**:896 (May 20) 1933.

50 Davidson, G. M. *Am. J. Psychiat.* **91** 41 (July) 1934.

51 Shulack, N. R. *Psychiatric Quart.* **12** 282 (April) 1938.

52 Sudden "Exhaustive" Death in Excited Patients, editorial, *Brit. M. J.* **2** 751 (Oct. 8) 1938.

53 Collins, R. T. *Bull. Neurol. Inst. New York* **7** 291 (Dec.) 1938.

most of the surface of the limbs after his eleventh three hour treatment with the Vapotherm at a temperature of 104 F Collins noted that anoxia or alkalosis might explain the findings His final conclusion was

Hyperthermia is a powerful therapeutic agent and may do injury to nervous tissue

In this section, many conditions outside the field of ophthalmology have been discussed An attempt has been made to indicate that "shock" therapy produces lesions which resemble pathologically the ocular lesions attributed to allergy All these accidents are manifestations of tissue anoxia All can be the result of varying degrees of arteriolar spasm and increased capillary permeability Many can be attributed to histamine Histamine is probably the cause of many ocular and extraocular allergic lesions Allergic lesions are due to capillary anoxia, the symptoms are due to the resulting tissue anoxia It does not seem reasonable to treat allergic lesions of the eyes with therapeutic agents which not infrequently cause similar ocular or extraocular lesions in persons previously free of such lesions As Horder <sup>54</sup> said in 1933 regarding shock therapy, some modern treatments consist in "seeing what can be done by direct action severed from physiological principles"

#### ACUTE CONGESTIVE GLAUCOMA

During the past fifteen years many clinicians have stated that acute glaucoma can be regarded as a localized intraocular vascular catastrophe Because epinephrine caused dilatation of the pupil of the sound eye in 12 of 15 cases of unilateral glaucoma, Knapp <sup>55</sup> concluded that susceptibility to epinephrine might be present long before the usual clinical signs of glaucoma were apparent Gifford <sup>56</sup> stated the opinion that vascular disturbances are important and that the effects of nervous influences on ocular tension are probably mediated by an action on the blood vessels, especially the capillaries Changes in blood chemistry may alter capillary permeability, swelling of the vitreous may be a factor, and low grade "inflammation" may play a part by producing venous stasis or increased capillary permeability or both Gifford also stated that several factors may play a role in any given case, accounting for the clinical differences among patients and their variable response to treatment

In 1931 Goldenburg <sup>57</sup> gave the results of a study of 12 cases of congestive glaucoma Every case presented definite evidence of altera-

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<sup>54</sup> Horder Brit M J **1** 859 (May 20) 1933

<sup>55</sup> Knapp, A Arch Ophth **50** 556, 1921

<sup>56</sup> Gifford, S R The Pathogenesis of Glaucoma, Arch Ophth **3** 88 (Jan) 1930

<sup>57</sup> Goldenburg, M Am J Ophth **14** 944 (Sept) 1931

tion of the vascular system, such as changes in the capillaries of the skin, increased blood pressure, sclerosis of the larger thoracic vessels, asthma (in 1 case) and hay fever (in 1 case) His conclusion was

the inherent cause of glaucoma lies in alterations in the capillaries, particularly of the ciliary body, these alterations consisting of an increase in permeability with a resulting swelling of this body, thus encroaching on the avenues leading to the canal of Schlemm

In an earlier paper Goldenburg<sup>58</sup> mentioned that this abnormal dilatation and permeability of the uveal capillaries were due to a stimulus which might be toxic, hormonal or nervous

Friedenwald<sup>59</sup> discussed 11 eyes which had been removed after attacks of acute glaucoma In the earlier and more acute stages serous, hemorrhagic and fibinous extravasations were present in the ciliary processes He attributed the intraocular pathologic process to a capillary poison because immediately after a tension-reducing operation on such an eye massive edema of the conjunctiva often occurs He found that intracutaneous injection of aqueous from an eye with acute glaucoma into the same patient caused an urticaria-like wheal to form, which increased in diameter from 3 to 7.5 mm in seventeen minutes Normal aqueous and saline solutions did not produce similar whealing He concluded<sup>59</sup>

Since no lesions of larger vessels were found, one must conclude that the extravasations and the edema fluid are derived from the capillaries Since capillary walls are known to be impermeable normally to the protein elements of the blood plasma, the permeability of the capillary walls has been increased

Vasomotor influences cannot be eliminated, but in some cases of acute glaucoma a transportable vasotoxic substance is demonstrably present in the intraocular fluids Whether this is the cause or the result of the glaucoma cannot at present be determined

Friedenwald and Pierce<sup>60</sup> also reported that injection of histamine into the vitreous of animal eyes caused a prompt and prolonged rise in tension, followed by a fall to below normal When histamine was injected into the anterior chamber, there was a rise in tension of short duration, a fall and then a second rise to normal or above normal, and there was also edema of the cornea and conjunctiva They noted that when different animals of the same species were given the same dose of histamine under conditions as nearly identical as possible pro-

<sup>58</sup> Goldenburg, M. *Am J Ophth* **11** 290 (April) 1928

<sup>59</sup> Friedenwald, J. S. The Pathogenesis of Acute Glaucoma. I. Clinical and Pathologic Study, *Arch Ophth* **3** 560 (May) 1930

<sup>60</sup> Friedenwald, J. S., and Pierce, H. F. The Pathogenesis of Acute Glaucoma. II. Experimental Study, *Arch Ophth* **3** 574 (May) 1930

found variations in the degree of reaction were observed. This last fact, I believe, speaks for a variation in hypersensitivity to histamine.

In my opinion, the sudden release at operation of aqueous containing histamine or a histamine-like substance explains the not uncommon development of acute glaucoma in the second eye shortly after operation on the first eye. In these cases the arterioles and capillaries are hypersensitive to histamine, and the vessels in the ciliary body are more sensitive than those in other tissues of the body. It is not unlikely that acute glaucoma and acute cyclitis are closely related. Glaucoma, however, is a capillary rather than an arteriolar disease. Because it often occurs in persons of the older age group, the arterioles, having thickened walls, cannot go into complete spasm. Acute glaucoma represents prestasis and/or stasis. Cyclitis and iridocyclitis are due to both arteriolar spasm and increased capillary permeability. These are manifestations of peristasis, or leukostasis. In acute glaucoma the eye is hard and the condition is analogous to an urticarial wheal. Because the arterioles are relatively patent, fluid can reach the capillaries, where it leaks out. In iridocyclitis there is also arteriolar spasm, little or no fluid gets to the capillaries, so it cannot leak out into the ciliary body and aqueous in large quantities, and hypotony occurs. Atropine is of value in the treatment of iridocyclitis, it is also indicated in the postoperative treatment of acute glaucoma. Is this because atropine has the side effect of dilating blood vessels?

My only criticism of the experimental work of Friedenwald and Pierce is that clinical conditions were not duplicated. If histamine is the cause of acute glaucoma, I think that it is formed elsewhere in the body and then transported by the blood to the ciliary body, where it first acts on the capillaries, and possibly the arterioles, causing edema of the ciliary body, and that its occurrence in the aqueous is secondary, not primary. Injection of histamine into the vitreous or the aqueous does not simulate clinical conditions.

In 1933 Duke-Elder<sup>61</sup> stated that a histamine-like substance could explain the rise of intraocular pressure which occurs after one produces total cessation of the intraocular circulation and that this substance was related to the H-substance of Lewis. He noted that axon reflexes, initiated by stroking the iris, caused a rise of tension in animal eyes. Presumably, axon reflexes and antidromic impulses liberate histamine at sensory nerve endings. While I agree with Duke-Elder that histamine can produce hypertension of the eye, I think that stopping the circulation produced intraocular anoxia and that this would suffice to cause increased capillary permeability.

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61 Duke-Elder, W. S. *Brit. M. J.* 1: 879 (May 20) 1933.

A year later Evans and Evans<sup>62</sup> stated

The essential lesion in acute congestive œdema may be said to be an "angio-neurotic œdema oculi" This might be more specifically defined as chemico-nervous

Venous stasis appears to be the primary factor, but it may be secondary or at least only contributory to arteriolar contraction and capillary dilatation and increased permeability, due to disturbance of the sympathetic and parasympathetic balance of the innervation of these vessels A further factor may be the presence in excess of histamine bodies in the capillary area

the trigger action which results in stasis and capillary transudation is supplied by nervous impulses from the higher centers or from peripheral nerve impulses and antidromic impulses

They also mentioned that epinephrine may constrict arterioles temporarily but that secondary congestion often follows its use

After stating that histamine causes both arteriolar constriction and increased capillary permeability, they suggested<sup>62</sup>

release of histamine in the tissues is an important exciting factor in the initiation and maintenance of the angioneurotic œdema of the eye which constitutes congestive glaucoma

Acetyl-choline is the physiological antagonist of adrenalin [and of histamine]. It produces dilatation of arterioles and constriction of capillaries It is for these reasons that it reduces venous congestion and capillary stasis

They mentioned the hypothesis, well known today, that physostigmine enhances the effect of acetylcholine by inhibiting the esterase and that the substance causing contraction of the pupil and dilatation of the arterioles may well be not physostigmine itself but acetylcholine, the survival of which it promotes These authors then reported several cases of acute glaucoma in which more or less temporary benefit was obtained with subconjunctival or intramuscular injections of acetylcholine

In a more recent article, Evans<sup>63</sup> stated that the causes of acute congestive glaucoma are those of capillary and venous stasis and that the ocular changes are due to a disturbance of the local circulation. Decompensation of the production of aqueous or its removal from the eye is the only feature common to a number of distinct conditions He also located the essential pathologic process in the capillaries and venules Emotional instability at the menopause or later and the action of hormones on blood vessels are also factors Arteriosclerosis probably plays a role The factors involved may be central or blood borne, as in the case of hormones, "toxins," vitamins and histamine Closure of the filtration angle is a secondary result of glaucoma, but an important complication

<sup>62</sup> Evans, J J, and Evans, P J Tr Ophth Soc U Kingdom 54 527, 1934

<sup>63</sup> Evans, P J Brit J Ophth 23 745 (Dec) 1939



Weinstein<sup>64</sup> could find no relation between hypertension and glaucoma. He agreed with Muller and Parrisius, who showed by capillaroscopy that the vasomotor instability of glaucomatous patients is a characteristic peculiarity. Moreover, he stated that the acute capillary dilatation observed during attacks of glaucoma is possible only with an elastic vessel wall, and not with the rigid, brittle walls of arteriosclerosis. He noted that of 3,254 glaucomatous patients 60 per cent were women and that 80 per cent of the acute attacks occurred in women at the time of the climacteric. Because of the preponderance of cases in women Weinstein expressed the belief that an endocrine factor is important. During the climacteric there is vasomotor instability, as shown by "congestion," perspiration and other vasomotor reactions.

He also mentioned the relation of glaucomatous attacks to cold weather and noted that this indicates vasomotor instability of the capillaries. Bruckner<sup>65</sup> had commented earlier on this well known relationship, mentioned in 1902 by Steindorff, who said that cooling of the body produced a disturbance in blood flow. Bruckner stated that sensitiveness to weather is an individual insufficiency which tends to increase with age. The work of Horton, Brown and Roth,<sup>66</sup> who proved that hypersensitivity to cold is due to histamine produced in the skin and carried by the blood to other parts of the body, would seem to indicate that histamine is the responsible agent in cases of acute glaucoma associated with chilling of the face or body.

Luedde<sup>67</sup> recently said that glaucoma is an intraocular edema with inadequate drainage and may be caused by general or local conditions which influence capillary permeability or obstruct the drainage of aqueous. He stated that capillary permeability may be affected by vasomotor disorders related to nervous or chemical stimuli, to posture or to trauma, as well as by toxic or nutritional alterations of the blood plasma, which may alter the intracapillary colloid osmotic pressure of the blood.

Kirwan,<sup>68</sup> in reporting on glaucoma in cases of epidemic dropsy, noted that the dropsy was due to eating rice which contained a toxin apparently formed by a spore-forming, gram-positive proteolytic bacillus of the vulgatus group, which is commonly found in diseased rice. The bacillus was found in the urine and stools of a number of patients. This

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64 Weinstein, P. *Brit M J* **1** 436 (March 4) 1939.

65 Bruckner, A. *Physiologic and Clinical Ophthalmologic Problems in Relation to Individual Variability*, *Arch Ophth* **20** 912 (Dec.) 1938.

66 Horton, B. T., Brown, G. E., and Roth, G. M. *Hypersensitiveness to Cold* *J A M A* **107** 1263 (Oct 17) 1936.

67 Luedde, W. H. *Am J Ophth* **23** 388 (April) 1940.

68 Kirwan, E. W. O'G. *Primary Glaucoma—A Symptom of Epidemic Dropsy*, *Arch Ophth* **12** 1 (July) 1934.

toxin is "soluble in water, resembles histamine and causes a 'cardio-capillary crisis'" A vitamin deficiency may have been the basic factor. Since all patients with epidemic dropsy do not have glaucoma, Kirwan stated that in some cases "the toxins showed a special predilection for the intraocular endothelium"

Later, Kirwan and Mukerjee<sup>69</sup> assumed that a toxic agent in the plasma produced the capillary dilatation and increased capillary permeability of glaucoma associated with epidemic dropsy. They referred to Chopra and De, who found a histamine-like base in the blood in cases of epidemic dropsy.

Also, Ridley<sup>70</sup> noted that Ryecroft, in 1934, found a vasotoxic substance in the aqueous in 3 out of 4 cases of acute glaucoma. Ridley stated that this substance resembled histamine.

Kraupa<sup>71</sup> reported on a condition he called glaucoma allergicum. This was a serous cyclitis with opacities in the vitreous and keratic precipitates but without posterior synechias.

Weekers and Barac<sup>72</sup> presented a case which they considered one of Quincke's edema inside the eye. Both eyes were lost. They suggested the term "paroxysmal intraocular edema" to differentiate the condition from cyclitis and other forms of glaucoma. They referred to Kraupa's case and mentioned a case of Baillart's in which there was edema of the conjunctiva that underwent variations parallel to those of the glaucoma.

Schroeder<sup>73</sup> explained the various stages of glaucoma on the basis of nutritional edema. He expressed the belief that the active stage of acute glaucoma is an angioneurotic edema of the eye. Among probable etiologic factors he includes protein deficiency, faulty assimilation, anemias resulting from infection, nutritional disturbances and hemorrhage, and possibly B avitaminosis.

Schoenberg<sup>74</sup> stated that acute glaucoma could be due either to a failing parasympathetic or to an overactive sympathetic nervous system or to a combination of the two. In cases of acute glaucoma associated with emotional upsets which he<sup>75</sup> reported the condition probably was due either to sympathetic overaction or to large amounts of epinephrine in the blood stream. Moon,<sup>26</sup> however, stated that the effect of large doses of epinephrine is similar to that of histamine in that the prolonged

69 Kirwan, E. W. O'G., and Mukerjee, S. N. *Brit J Ophth* **22** 329 (June) 1938.

70 Ridley, F. *Tr Ophth Soc U Kingdom* **58** 590, 1938.

71 Kraupa, E. *Arch f Augenh* **109** 416 (Dec.) 1935.

72 Weekers, L., and Barac, G. *Arch d'opht* **1** 193 (March) 1937.

73 Schroeder, H. *New Orleans M & S J* **87** 671 (April) 1935.

74 Schoenberg, M. *Brit J Ophth* **22** 417 (July) 1938.

75 Schoenberg, M. J. *Role of States of Anxiety in the Pathogenesis of Primary Glaucoma*, *Arch Ophth* **23** 76 (Jan.) 1940.

vasoconstriction causes capillary anoxia with increased capillary dilatation and permeability

*Therapy*—Besides physostigmine, pilocarpine and acetylcholine, other drugs have been used for acute glaucoma. Thiel and Heim instituted the use of ergotamine tartrate, which probably acts by paralyzing the motor endings of the sympathetic nervous system. Josephson<sup>76</sup> reported good results with adrenal cortex extract. This is presumed to act by regulating salt metabolism and decreasing capillary permeability. Woods<sup>77</sup> could not confirm Josephson's work. Hamburger, Gifford and others have used epinephrine. Hypertonic solutions of dextrose or sucrose have been recommended by other workers. Paul,<sup>78</sup> and later Miller,<sup>79</sup> used splenic extract because Paul considered that acute glaucoma was a manifestation of allergy and because splenic extract had been helpful in some cases of urticaria. Clarke<sup>80</sup> used mecholyl and neostigmine, which act similarly to acetylcholine and physostigmine.

Rabinowitch<sup>81</sup> tried a totally different type of therapy. Instead of using drugs which act on the sympathetic or the parasympathetic nervous system, he used amyl nitrite, which acts directly on the arteriolar walls and is a vasodilator. He reported 16 cases of glaucoma (9 of acute inflammatory glaucoma, 3 of chronic inflammatory glaucoma and 4 of simple glaucoma), with inhalations of amyl nitrite 13 patients showed improvement. The patients with acute inflammatory glaucoma responded best, and those with simple glaucoma showed no response. Because the action on the tension was not permanent, Rabinowitch recommended amyl nitrite only for interrupting the attack.

From a brief consideration of these few recent articles, it is apparent that the idea of acute glaucoma being primarily due to capillary dysfunction has been slowly developing. Many investigators consider it to be an angioneurotic edema. Many have implicated histamine or histamine-like bodies as the etiologic agent. Others prefer the theory of an autonomic imbalance. Changes in weather seem to play a role, but histamine accounts for the glaucoma in these cases. Endocrine influences also probably act via the arterioles and capillaries by raising or lowering the threshold of response to vasomotor stimuli. If protein

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76 Josephson, E. M. *Eye, Ear, Nose & Throat Monthly* **13** 453 (Jan) 1935

77 Woods, A. C. *The Use of an Extract of Adrenal Cortex in Glaucoma*, *Arch Ophth* **14** 937 (Dec) 1935

78 Paul, T. M. *Urol & Cut Rev* **38** 207 (March) 1934

79 Miller, E. A. *Am J Ophth* **22** 536 (May) 1939

80 Clarke, S. T. *Am J Ophth* **22** 249 (March) 1939

81 Rabinowitch, M. G. *Soviet vestnik oftal* **7** 181, 1935, abstracted, *Arch Ophth* **15** 936 (May) 1936

allergy is the cause, the antigen-antibody reaction liberates histamine or a histamine-like body. Lack of the vitamin B complex means lack of nicotinic acid, a vasodilator, and lack of thiamine, which is said to potentiate the action of acetylcholine by neutralizing esterase.

Since allergy is a manifestation of altered permeability of membranes or of smooth muscle spasm, it is obvious that acute congestive glaucoma can also be considered allergic. All substances, whether of chemical, nervous or endocrine origin, which, by virtue of their presence or their absence, alter capillary permeability or cause arteriolar spasm are possible etiologic agents. Since oxygen is most important for maintaining normal capillary permeability, and since ordinarily the blood contains sufficient oxygen, it is apparent that acute glaucoma is a manifestation of localized capillary and tissue anoxia.

Two factors operate to produce glaucoma: first humoral or nervous influences, which act like histamine in causing either arteriolar spasm or increased capillary permeability or both, and, second, hypersensitivity of the vascular system of the ciliary body to these influences. The rise in tension is a secondary effect, depending on a number of variables, such as size and position of the lens, the effect of a dilated pupil on the filtration angle and, probably, the rate at which the leaking capillaries allow fluid to pass into the ciliary body.

In all cases glaucoma can be regarded as due to failure of homeostasis, but not in all cases is the condition due to the same etiologic agent, and in many cases several etiologic factors are concerned.

Furthermore, all drugs which seem to be of value in lowering the tension act directly on arterioles. Most of them also act on the sphincter iridis. In the past it has been assumed, perhaps wrongly, that the pupillary responses were of major importance. For that reason, the reports of Evans and Evans and of Rabinowitch are of fundamental interest. Amyl nitrite acts only on arterioles. Moreover, as Pickering<sup>80</sup> reported, amyl nitrite quickly abolishes the headache which results from the intravenous injection of histamine. In addition, Drinker and Bronfenner,<sup>82</sup> cited by Seegal reported that amyl nitrite caused relaxation of the constriction of the pulmonary vessels which occurs in the rabbit in anaphylactic shock, and they concluded that the arterioles were the site of the spasm. Since anaphylactic shock is assumed by many workers to be due to histamine, it is apparent that glaucoma can be a manifestation of allergy, since a histamine origin explains many cases. In those cases in which the glaucoma is not attributable to histamine, other factors affecting the arterioles or capillaries can be blamed as etiologic agents. All drugs which relieve glaucoma also have arteriole-dilating properties. Amyl nitrite has a dilating action

<sup>82</sup> Drinker and Bronfenner, cited by Seegal<sup>16</sup>

on the arterioles, yet it is effective in temporarily relieving acute glaucoma, in aborting histamine headache and in relieving some of the effects of anaphylactic shock. The pathology of histamine is the pathology of allergy, and both agents cause capillary and tissue anoxia. The physiologic antagonists of histamine are the physiologic antagonists of allergy, and all these physiologic antagonists relieve tissue anoxia by improving the supply of oxygen-containing blood to the anoxic tissues. Which cases of acute glaucoma are due to protein allergy (histamine resulting from antigen-antibody reaction) and which to physical allergy (histamine formed by action of cold on the skin) or to overaction of the sympathetic nervous system cannot always be determined. Whatever may be the cause of acute glaucoma, the disease is a manifestation of capillary and tissue anoxia. Meyer and Cook<sup>83</sup> have stated that defective tissue oxygenation is often merely a final common pathway of etiologically different disease processes.

#### HERPES

The various types of herpes of the cornea, as well as herpes zoster ophthalmicus, can be attributed to a lesion in the gasserian ganglion. In cases of dendritic keratitis, such a lesion accounts for the diminished corneal sensitivity, as well as the intense pain and headache, both of which are out of proportion to the extent of the corneal lesion.

Moore,<sup>84</sup> in discussing herpes zoster ophthalmicus, said

If the patient has died with the eruption still out upon the skin, the affected ganglion will be found to be in a condition of profound inflammation, with areas of extravasated blood, or if the patient has died quite early, the blood may be seen with the naked eye. Similar changes are present in that part of the sheath which covers the diseased portion of the ganglion, the vessels are engorged, blood is extravasated, and the sheath is invaded by multitudes of small round, deeply staining cells. As soon as the inflammation has expended itself absorption begins, and ultimately the focus becomes converted into fibrous tissue, within this area all ganglion cells and nerve fibers are destroyed and the overlying sheath is thickened.

Paton<sup>85</sup> mentioned the same changes, his description being based on Head and Campbell's report in 1900. These herpetic lesions have been attributed to a virus, to allergy, to foci of infection and to toxemia. The pathologic process is the same as that of anterior poliomyelitis, but sensory rather than motor nerve cells are involved. Paton mentioned that the corneal and cutaneous lesions have been attributed to interference with trophic nerve fibers and to vasomotor changes.

Many physiologists have mentioned that "irritation" of the posterior root ganglions sets up antidromic impulses which cause the peripheral

83 Meyer, A., and Cook, L. C. *J. Ment. Sc.* **83** 258 (May) 1937.

84 Moore, R. F. *Medical Ophthalmology*, ed 2, London, J. & A. Churchill 1925.

85 Paton, L. *Brit. J. Ophth.* **10** 305 (June) 1926.

cutaneous lesions of herpes zoster. If one agrees that antidromic impulses release H substance or histamine, one has an explanation for the peripheral lesions. What causes the primary changes in the ganglion?

The pathologic changes in the ganglion are basically similar to those of episcleritis, retrobulbar neuritis and closure of the central retinal artery. There are edema, round cell infiltration, extravasations of red blood cells and capillary dilatation. In other words, varying degrees of prestasis, peristasis and stasis occur. This is the pathology of allergy. The fact that the gasserian ganglion is concerned with relaying sensory impulses centrally accounts for the pain in the eye, headache, disturbances in the skin and corneal sensitivity. The fibrous sheath of the ganglion prevents any expansion of the edematous tissue, so pain is outstanding, even when only the sensory fibers to the cornea are involved. Herpes of the cornea and herpes zoster ophthalmicus differ probably only in the location and size of the lesion in the ganglion.

The factors predisposing to herpes are similar to those for other allergic lesions of the eye. Among these factors are head colds, infections of the upper respiratory tract, exposure to cold, "toxemia" and a sudden change in the meteorologic environment.

In my opinion, the changes in the ganglion are manifestations of tissue anoxia. Herpes due to cold and allergy is as likely to be due to histamine as are choroiditis, retrobulbar neuritis and scleritis. Herpes is analogous to acute glaucoma except that the one involves the eye whereas the other involves a ganglion. Both can be considered as manifestations of an angioneurotic edema.

Capillary permeability is increased in association with herpes. This change may be due either to arteriolar spasm or to primary changes in the capillary endothelium. Either histamine or a histamine-like body can account for these vascular changes in the ganglion. Either the increased intraganglionic pressure or the tissue anoxia or both in some way initiate antidromic impulses which cause the cutaneous and ocular lesions. Such a conception of the herpetic lesion provides for a self-perpetuating mechanism due to a nonliving chemical substance. Histamine produced anywhere in the body acts on the gasserian ganglion. Antidromic impulses are initiated which liberate H-substance (histamine?) and cause the distant cutaneous and ocular lesions. The histamine liberated peripherally not only accounts for the peripheral lesions but may be absorbed and either intensify and continue the process in the ganglion or cause vascular lesions in any other tissue of the body where there are histamine-sensitive cells. Such an interpretation adequately explains lesions attributed to viruses as manifestations of disordered physiologic functions.

Four cases are reported briefly in which only therapy directed toward relieving the localized tissue anoxia was used. In other cases similar treatment has met with equally good results, but these 4 instances will suffice to indicate the value of vasodilator therapy for herpes.

CASE 1—Mrs. R. R., a woman aged 34, was seen on Dec. 20, 1939, with severe herpes zoster ophthalmicus involving the left side of the forehead. There was also one vesicle on the left upper lid, this lid was extremely edematous. The lesions had been present for five days. The pain was unbearable and had not been relieved with sedatives and local applications to the skin. The left eye, which was normal, was not affected.

The only cause ascertainable was exposure to cold. On December 13, after having her hair washed, she had gone out in the cold and "taken in" a neighbor's washing. She had been thoroughly chilled after this and had experienced great difficulty in getting warm after the exposure.

She was given 0.1 Gm. of sodium nitrite intravenously on December 20, 21, 22 and 23 and 30 mg. of erythrityl tetranitrate twice daily from December 21 to Jan. 5, 1940. On December 21 the pain was less severe, on December 22 there was no pain, the edema of the lid had decreased and she could tolerate firm pressure on the left side of the forehead. On December 23 she had no subjective complaints, and the vesicles had started to regress. They disappeared in about ten days. There have been no recurrences.

CASE 2—R. S., a girl of 9, was seen on April 1, 1940 with the complaint that the left eye had been red and irritated for eleven days. One week before the eye was involved she had had a head cold.

Vision in the left eye was 20/70—, and the eye was soft. There was pronounced circumcorneal injection. On the cornea there were several superficial, grayish vesicles, which stained at their apexes. The cornea was hazy, and the sensitivity was greatly reduced. The markings of the iris were indistinct, and a few dilated blood vessels could be seen on the iris. The patient complained of severe pain in the eye and headache on the left side. Photophobia was intense. Atropine salve was placed in the conjunctival sac, and the patient was given 70 mg. of sodium nitrite intravenously on April 1, 2, 3 and 6.

Improvement was rapid. On April 2 the pain had disappeared, the ocular tension had improved, the circumcorneal injection was less noticeable and corneal sensation had improved. On April 6 the eye was nearly white. On April 10 vision was 20/20, the eye was completely white, corneal sensation was normal and the corneal lesions were represented by tiny subepithelial opacities. There have been no recurrences.

This case was one of herpes corneae with mild herpetic iritis. Vasodilators caused immediate relief of the symptoms, and the ocular lesions regressed rapidly. Because of the photophobia, this patient received atropine for six days.

CASE 3—R. M., a man of 23, was seen on May 7, 1940. He complained of tearing and photophobia in the right eye with severe pain in and behind that eye. He had spent May 5 in a mountain camp, where it had been very cold in the evening. On May 6 the aforementioned symptoms developed, and there were also symptoms of a mild "head cold."

Vision in the right eye was 20/25— Photophobia and tearing were pronounced. There was moderate circumcorneal injection, the corneal sensitivity was reduced, and in the pupillary region of the cornea there were three elevated, grayish lesions, which did not stain. The iris was greenish, its markings were blurred, and there were a few cells in the anterior chamber. The left eye was amblyopic.

This patient received 0.1 Gm of sodium nitrite intravenously on May 7, 8, 9, 10 and 11, and 30 mg of erythrityl tetranitrate each evening from May 7 to May 13. A drop of scopolamine hydrobromide was instilled in the conjunctival sac on May 7, 8 and 9. The eye was not covered with a patch.

On May 8 the photophobia, tearing and redness were less intense. On May 9 the aqueous was free of cells, and the iris was less greenish. There was still a faint circumcorneal injection. The patient had no subjective complaints. On May 11 the eye was completely white. One tiny gray opacity was present in the pupillary region of the cornea, this opacity was definitely subepithelial. There have been no recurrences to date.

In this case, which was similar to case 2, cure occurred in four days after intensive vasodilator therapy, which was directed toward the lesion in the gasserian ganglion rather than toward the secondarily involved cornea and iris.

CASE 4—J. H. S., a man of 47, was seen on Jan. 15, 1944. On or about Jan. 1, 1944 herpes zoster ophthalmicus developed on the left side. On January 11 the left eye became painful, vision was foggy and there was lacrimation.

On examination (January 15) he had one herpetic vesicle at the hair line on the forehead, three on the left side of the forehead, one on the left side of the nose and one on the columella of the nose. There was moderate pain in the affected region.

Vision in the left eye was 20/70— and was not improved with any lens. There was a faint circumcorneal injection, and the whole cornea had a whitish, pebbly appearance, due to deep keratitis. After dilation of the pupil a faint red reflex was obtained, but no details of the iris, optic nerve or retinal vessels could be observed. The field was grossly normal. The right eye was entirely normal.

Treatment consisted in administration of 100 mg of nicotinic acid three times a day after meals, 30 mg of erythrityl tetranitrate on retiring and 1 drop of 0.25 per cent scopolamine hydrobromide in the left eye twice daily.

On January 18 the cornea was clearer, so that it was possible to see deposits on its posterior surface. The pupil was in mid-dilation, and the iris was greenish. There were no synechias. There was a decrease in the pain in the region of the vesicles on the face.

On January 22 vision was 20/40 and the cornea was much clearer so that the deposits on the posterior surface of the cornea were clearly visible. The patient stated that improvement in vision had occurred on January 20 and that he was free of all pain.

On January 28 vision was 20/25 + 2, the eye was white, the deposits on the cornea were fewer, the media were clear and the fundus was normal. At this time the patient was pronounced clinically cured because he was entirely free of symptoms and the vesicles on the face had disappeared almost entirely.

He continued to take nicotinic acid by mouth for three weeks longer. On February 4 and February 18 vision was 20/16—3 and there were still deposits on the back of the cornea.



He was last seen on Nov 20, 1944. At this time vision was 20/16—2. The left pupil was slightly larger than the right, and there was some atrophy of the superior pupillary margin of the iris. The deposits on the posterior surface of the cornea had entirely disappeared.

This was a case of herpes zoster ophthalmicus with keratitis profunda and cyclitis. The most likely etiologic factor was exposure to cold weather. A clinical cure was obtained in thirteen days with the administration of vasodilators by mouth.

In my opinion, herpes zoster ophthalmicus, herpes corneae and herpes iridis are not diseases *sui generis* but are basically the same as other allergic lesions except that the primary pathologic process is located in the gasserian ganglion. A histamine origin accounts for both the central and the peripheral lesions. Whether the histamine is derived from the skin, an antigen-antibody reaction or a virus (?) cannot be determined. The development of herpes in 46.2 per cent of the 411 patients treated with artificial fever by Warren, Carpenter and Boak<sup>47</sup> offers much evidence for a histamine origin of herpes. Since the heating of tissues, as well as the cooling, results in the formation of histamine, there is no necessity for assuming that these ocular lesions are due to a virus. The various herpetic lesions of the eye are due to an acute vascular catastrophe in the gasserian ganglion. The pathology is that of allergy and also that of histamine poisoning. Therapy directed toward the assumed vascular changes (arteriolar spasm and increased capillary permeability) seems to be more effective than the customary methods. Such therapy, which acts by increasing the supply of oxygen-containing blood and thereby relieving the capillary and tissue anoxia, is based on physiologic principles and deserves a trial in similar cases.

#### PARALYSIS OF OCULAR MUSCLES

Appelbaum<sup>2</sup> referred to a case of Lemoine's in which the patient had attacks of diplopia, vertigo and scintillating scotoma without headache. Allergy to cheese was considered the cause because the attacks ceased after the patient eliminated cheese from his diet.

Kahoun<sup>86</sup> reported 8 cases of paralysis of one or more of the ocular muscles following influenza. In 1 case at the beginning of the influenza, all the muscles of the right eye became paralyzed, and this condition did not improve. Of the 7 remaining cases in which paralysis developed during convalescence and ran a benign course, bilateral perineuritis was present in 1 and typical retrobulbar neuritis in another.

Since many of the manifestations of influenza are due to diffuse, but mild, changes in the function of the arterioles and capillaries, and

<sup>86</sup> Kahoun, S. Ceskoslov oftal 3:109, 1937, abstracted, Am J Ophth 21:458 (April) 1938.

since influenza is considered to be a manifestation of allergy, it is apparent that Kahoun's cases represented instances of allergy with focal areas of edema in the oculomotor nerves or in the oculomotor nuclei, as well as in the optic nerves. Had the optic and retrobulbar neuritis been accompanied with symptoms referable to the spinal cord, the diagnosis of neuromyelitis optica could have been made. Neuro-myelitis optica often follows an infection of the upper respiratory tract or influenza. When it does not, it is considered to be acute multiple sclerosis by some authorities.

Many patients with influenza complain of pains in the muscle and of muscular weakness. Possibly these are preclinical states of neuromyelitis optica. Moreover, the pathology of neuromyelitis consist in localized areas of softening and necrosis with perivascular lymphocytic infiltration. This is the pathology of allergy, and this is the stage which Ricker and Krogh would characterize as peristasis, or leukostasis. It is also the pathology of acute retrobulbar neuritis.

If multiple sclerosis is due to allergy, as suggested by Kennedy<sup>87</sup> and many others, or if it is a primary vascular disease, as asserted by Oppenheim<sup>88</sup> in his textbook many years ago, all the manifestations of this disease are of either allergic or vascular origin. If vascular, they may be manifestations of allergy. In many cases of paralysis of isolated extraocular muscles the cause may be angiospasm. These cases may be examples of monosymptomatic multiple sclerosis.

Kennedy, Wortis and Wortis<sup>89</sup> also noted that vascular accidents occur in the brain in cases of untreated syphilis, and they attributed such accidents to angiospasm.

Assuming that the various types of paresis of ocular muscles may be allergic and due to angiospasm, with resulting capillary and tissue anoxia, I wish to report 7 cases in which only vasodilators were employed. Whether the pathologic process was located in the nerves or the nerve centers could not be determined. It was probably not located in the muscle substance itself.

CASE 1—R. N., a man of 60, was seen on Aug. 29, 1938 with paresis of the right internal rectus muscle, of two days' duration. He could adduct the right eye 30 degrees to the left. On September 9, after eight intravenous injections of sodium nitrite (0.1 Gm.) and oral administration of erythryl tetranitrate, he was free from symptoms and could adduct the right eye 60 degrees to the left without the occurrence of diplopia. The Wassermann reaction of the blood was strongly positive, so he was referred for antisiphilic treatment, after partial paralysis of the third nerve was cured.

<sup>87</sup> Kennedy, F. *New York State J. Med.* **36** 469 (April 1) 1936.

<sup>88</sup> Oppenheim, H. *Diseases of the Nervous System*, translated by E. E. Mayer from the second German edition, Philadelphia, J. B. Lippincott & Co., 1900.

<sup>89</sup> Kennedy, F., Wortis, S. B., and Wortis, H. *New York State J. Med.* **38** 1441 (Nov. 15) 1938.

CASE 2—M B, a Negro of 42, was seen on Nov 14, 1938 with the complaint of double vision, present for ten days. He had almost complete paralysis of the left external rectus muscle and could abduct the left eye only 10 degrees beyond the midline. He received nine daily injections of sodium nitrite. On November 18 he could abduct the left eye 40 degrees beyond the midline, with both eyes open, diplopia did not occur until he rotated his eyes 50 degrees to the left. On November 23 he could abduct the left eye 60 degrees beyond the midline. The Wasserman reaction of the blood was 4 plus. He began to receive anti-syphilitic treatment on November 18, at which time he had recovered at least 50 per cent of the lost function of the external rectus muscle.

CASE 3—J K, a man of 68, was seen on Jan 24, 1938 with paralysis of the left external rectus muscle, present for twenty-three days. The left eye could not be abducted beyond the midline. He received nine daily intravenous injections of sodium nitrite (0.1 Gm). He could abduct the left eye 30 degrees beyond the midline on February 2, 40 degrees on February 18, 50 degrees on March 11 and 60 degrees on March 18. At the last visit he had only a trace of diplopia in gazing to the extreme left. This patient's improvement began coincidentally with the institution of vasodilator therapy. Fifty-three days after treatment was started he had recovered normal function.

CASE 4—B W, a man of 45, was seen on Aug 14, 1937 with complete paralysis of the left external rectus muscle, present for five days. After twenty daily intravenous injections of sodium nitrite (0.1 Gm) he could abduct the left eye normally without diplopia. The Wassermann reaction of the blood was negative.

CASE 5—S S, a woman of 25, with advanced multiple sclerosis, nystagmus and bilateral temporal optic nerve atrophy, had onset of paralysis of the elevators of both eyes on May 28, 1938. She received twelve daily intravenous injections of sodium nitrite. Twenty days after the onset of the attack she could elevate her eyes normally. The nystagmus was unchanged.

CASE 6—J D, a man of 34, was seen on Nov 16, 1938 with paresis of the left external rectus muscle, present for several days. He could abduct the left eye 25 degrees beyond the midline with difficulty and had diplopia in the whole field of that eye. On November 28, after ten intravenous injections of sodium nitrite, he could abduct the left eye 45 degrees, diplopia began before this point was reached. He failed to return for further treatment.

CASE 7—H M, a man of 30, was seen on Oct 18, 1937 with paresis of the left external rectus muscle, present for ten days. At the onset he had a head cold. Diplopia occurred when the left eye was abducted 20 degrees. After four daily intravenous injections of sodium nitrite, he could abduct the left eye 30 degrees before diplopia occurred. He stated that he was much better. Because the Wassermann reaction was strongly positive, he was referred elsewhere for treatment. He did not return. This patient showed improvement, and vasodilator therapy should have been continued, as it was in case 1.

Of necessity, controls are difficult to obtain. In 1933 Agatston<sup>90</sup> reported 4 cases of paralysis of the external ocular muscles. Treatment consisted of injections of a bismuth compound, administration of mercury and potassium iodide by mouth and weekly catharsis. The Wassermann reaction was negative in all cases. The patients' ages

90 Agatston, S. A. M. J. & Rec **138** 41 (July 19) 1933

were 50, 38, 59 and 73 respectively, all were men. The muscles involved were, respectively, the internal rectus, the superior oblique, the superior oblique and all muscles supplied by the third nerve. The patients were completely cured in three, six, six and three months, respectively. The third patient (aged 59) later had complete paralysis of the third nerve, with the aforementioned treatment he was cured in thirteen weeks.

The times required for cure in the first 5 of my cases were eleven, nine, fifty-three, twenty and twenty days, respectively. In the other 2 cases improvement occurred, but the patients did not remain under observation and treatment sufficiently long for therapy to be considered either a success or a failure. Dr Michael Goldenburg has informed me that a patient with paresis of the sixth nerve responded to this treatment.

Agatston used mercury and bismuth preparations and iodides because the ocular muscles are often paralyzed in cases of syphilis and these drugs help to cure the syphilis and the ocular paralyses. I used vasodilators because I believe many of these paralyses are of vascular origin, whether due to allergy, syphilis or other factors. The times of cure were much shorter for the patients treated with vasodilators than for those treated with mercury, bismuth and iodides. In my opinion, the time required for cure must be considered in attempting to evaluate the results of therapy.

#### RETINA

Serum sickness is considered a manifestation of allergy or anaphylaxis. Over fifteen years ago Brown,<sup>44</sup> in discussing serum sickness in man, said

The lesions and reactions in all species are probably fundamentally produced by the same mechanisms, and differ by reason of the difference in anatomic structure and physiologic reactions. Thus, no one symptom or group can be said to be characteristic in all animals. There is one manifestation, however, that can be considered as an accompaniment in all instances of anaphylaxis of which serum sickness is a phenomenon, and that is *vascular dilatation with serous exudation*.

He stated that in serum sickness the initial rise in blood pressure may be due to vasoconstriction, which is followed by paresis and a fall in blood pressure. Then other signs of vasodilatation appear. "Hyperemia" with serous exudation and resulting edema is the most frequent and is, according to the organ or organs involved, the cause of most of the symptoms.

Brown also noted that the fundus presents for inspection a vascular tissue, which is represented by the choroidal vessels, the ciliary system and the retinal system, the disk presents nonmedullated nerve fibers

Therefore one can study at close range fundamental processes, such as vascular changes associated with nervous manifestations, *in vivo*

Brown reported the ocular reactions of 75 patients who received diphtheria antitoxin intravenously. Lacrimation and dilatation of the conjunctival vessels occurred frequently. Changes in the fundus included hyperemia of the disk and retina with elevation of the optic cup. The retinal veins and capillaries were dilated and definite papilledema developed in 20 per cent of cases. There was also a "watered-silk" appearance of the retina in the patients with the severer reactions. About 10 per cent of the patients complained of "blurriness" of vision. Administration of epinephrine had a very temporary effect on the ocular manifestations. The ocular changes cleared up in from four to twenty-eight hours. Experiments on 4 animals resulted in similar changes in the conjunctiva and fundus.

Brown concluded his article as follows <sup>44</sup>

The vascular manifestations are perhaps the most striking and the most important concerned. Hyperemia, then, must not be construed to indicate beginning inflammation of the disc, but a marked vasodilatation dependent on the serum reaction.

The direct action of the serum itself, as brought to the tissues, probably does not enter primarily into the ocular reaction. The primary response is a vascular one.

In Brown's cases, capillary dilatation and increased capillary permeability with resulting edema were the outstanding changes. He did not mention the retinal arteries except to say that in a few cases they showed increased tortuosity. Also, exudation from the choriocapillaris may have occurred.

Spastic closure of the central retinal artery or of one of its branches probably represents an allergic reaction in its simplest form, since the present study is concerned anatomically with only vascular and nerve tissue. There is a minimum of connective tissue, and the branches of the retinal artery are practically on the retina. The main trunk, the superior or inferior division or, finally, the nasal or temporal branch of either division may be affected, with involvement of each vessel the fundus picture is characteristic. The loss of function corresponds with the extent of vascular involvement. This is particularly true when only a cilioretinal artery is affected.

Kyrieleis <sup>91</sup> recently pointed out that the term "peristasis" was introduced by Ricker, who applied it to a functional process in the vascular system in which the capillaries were dilated and the arterioles contracted. Kyrieleis reported 3 cases of incomplete arteriosclerotic occlusion of the central retinal artery. Owing partly to organic and

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<sup>91</sup> Kyrieleis, W. "Peristatic" Conditions Associated with Incomplete Occlusion of the Central Artery, *Arch Ophth* **23** 447 (Feb) 1940.

partly to functional causes, a circumscribed narrowing of the arteriole was produced, and in the area supplied by the affected artery there was a circumscribed edematous swelling of the retina. In 1 case hemorrhages developed. Kyrieleis concluded that peristatic circulatory disturbances lead to extravasation of fluid and cellular constituents of the blood through the vessel walls and that the increased capillary permeability is caused by impaired nutrition.

In discussing Kyrieleis' report, Scheerer stated that peristatic hyperemia in cases of occlusion of the central retinal artery is more pronounced when there is no arteriosclerosis. Mylius then stated that he had observed in patients with eclampsia that peristatic conditions preceded the retinal changes.

Marucci<sup>92</sup> reported a case of bilateral retinal angiospasm in a woman of 38 who had been lactating for seven months. She also had nausea and dizziness and had increased in weight for several years. The capillary circulation in the nail beds was definitely pathologic. Acetylcholine and the use of an estrogenic preparation effected complete return of vision to normal. Marucci attributed not only the ocular signs but also the headache and vertigo to vascular spasm. He expressed the belief that ovarian dysfunction was the primary cause of the condition.

Geserick<sup>93</sup> reported the case of a man who from the age of 21 had had repeated intraocular hemorrhages. At 41 he had bilateral atrophy of the optic nerve. The threadlike retinal arteries were in part converted into white lines, the veins were attenuated, and there were chorioretinal lesions close to the vessels. There was no pulse in either dorsalis pedis artery, and neurologic examination led to a diagnosis of disseminated sclerosis. All the changes were attributed to endangitis obliterans.

This case was one of multiple sclerosis with repeated spasms of the retinal arteries rather than of the vessels supplying the optic nerve. The chorioretinal lesions were also probably due to local circulatory impairment. Whether the vascular spasms were due to allergic, nervous or climatic factors could not be determined from the report.

Bender<sup>94</sup> mentioned the case of a woman who had blurring of vision and diplopia within twenty-four hours after the extraction of four teeth. After thirty-six hours vision was reduced to 1/200 in the right eye, the left eye was totally blind. Clinically, the fundus picture was that of thrombosis of the central retinal vein. After six weeks both nerve heads were white and indistinct and the blood vessels

92 Marucci, L. *Ann di ottal e clin ocul* **64** 671 (Oct) 1936

93 Geserick, H. *Arch f Ophth* **138** 647, 1938, abstracted, *Am J Ophth* **21** 1061 (Sept) 1938

94 Bender, M. B. *Am J Ophth* **18** 148 (Feb) 1935

in the fundus were represented by a few whitish streaks radiating from the nerve heads

This case, in which spastic closure of the central retinal artery must have occurred, is similar to cases of iritis which develops after a focus of infection is opened up or removed. Whether these accidents are due to the flooding of the blood stream with allergins from the focus of infection or to the absorption of blood or to an axon reflex cannot be determined. The fundus picture in Bender's case was that of allergy (peristasis and stasis) and was a manifestation of tissue anoxia.

Toth and Meszaros<sup>95</sup> reported the case of a woman of 70 who on stepping out into the cold air suddenly became blind in the left eye. Later the fundus showed atrophy of the optic nerve and narrowing of the retinal arteries. In the right eye, vision was reduced to 5/15, green was not recognized, and the retinal arteries showed variations in caliber. For four years this patient had noticed that her fingers became white and numb in the cold. The capillaries in the nail beds were scarcely visible and the capillary blood flow was retarded. Vision improved to 5/7 (left eye) after fifteen daily intravenous injections of 10 cc of a 40 per cent solution of dextrose. In this case the ocular condition can be interpreted either as an allergic reaction to cold or as a pressor vasomotor reflex from the skin. Whatever the cause, exposure to cold was the inciting stimulus, and histamine could have caused the ocular lesions.

Rheumatic fever and chorea are considered manifestations of allergy. Bride<sup>96</sup> reported the case of a girl aged 8 years with chorea, who had closure of the central retinal artery in one eye. When Bride saw her, there was complete atrophy of the optic nerve. If chorea is primarily due to allergy and if closure of the central retinal artery in this patient was a manifestation of rheumatic fever, it is possible that many cases of closure of the retinal artery in young people may represent monosymptomatic rheumatic fever.<sup>1</sup> Moreover, inasmuch as vasodilator drugs are the most effective means of relieving spasm of the central retinal artery, they should be effective in aborting the carditis, arthritis and chorea of rheumatic fever if these conditions also are due to local vascular dysfunction secondary to allergy. I believe that they are.

In some cases detachment of the retina may be of vascular origin and a manifestation of localized anoxia. Several years ago I saw a man who had made many trips by airplane. Thrombosis of the central retinal vein developed in one eye, this cleared up. Later a detachment

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<sup>95</sup> Toth, Z, and Meszaros, K. *Klin Monatsbl f Augenh* **91** 815 (Dec) 1933

<sup>96</sup> Bride, T. M. *Tr Ophth Soc U Kingdom* **57** 346 1937

of the retina developed in the other eye. Each time he went aloft he became anoxic. Possibly the thrombosis of the central retinal vein and the detachment were due to localized anoxia secondary to the anoxemia. This viewpoint is not unreasonable, as de Roth<sup>97</sup> has noted that in cases of detachment a vascular degeneration is usually present. He referred to Vogt's theory that primary damage occurs in the vessels, not in the retina. If anoxemia can cause retinal detachment, then localized tissue anoxia due to arteriolar spasm and increased capillary permeability (which may be due to allergy) can also account for some cases of retinal detachment.

The literature contains many reports of the efficacy of vasodilators in curing spastic closure of the central retinal artery or one of its branches. Minton,<sup>98</sup> Butler, Pickard, Smith and many others have stated their belief that spasm explains the closure in many of these cases. Emboli do occur, as in the case of Orr and Young,<sup>99</sup> but are rare. In sclerosed vessels, which occur in the older age groups, spasm probably precedes a thrombotic occlusion, according to Minton. Tortella<sup>100</sup> stated that the form which responds to vasodilators is due to spasm and that the therapeutic response supplies the necessary data for differential diagnosis.

In conclusion, it is obvious that closure of the central retinal artery can be attributed to cold, stirring up of foci of infection, rheumatic fever, endocrine imbalance, multiple sclerosis and, probably, many other etiologic factors. The changes in the fundus are those of allergy and are attributable to smooth muscle spasm and increased capillary permeability. When allergy is viewed, not as hypersensitivity to allergins but as a vascular response to a number of etiologic factors, it must be apparent that closure of the central retinal artery, particularly in young people, gives the gross picture of allergy. Tissue anoxia results. Treatment directed toward the vascular spasm is the most effective means of treating this manifestation of allergy. Moreover, closure of the central retinal artery is comparable to acute exudative chorioiditis, acute iritis and iridocyclitis and acute retrobulbar neuritis.

#### OPTIC NERVE

The alleged causes of acute optic and retrobulbar neuritis include allergy, focal infection, pregnancy, lactation, endocrine disorders, multiple sclerosis and other demyelinating diseases and serous menin-

<sup>97</sup> de Roth, A. Bilateral Detachment of the Retina, *Arch Ophth* **22** 809 (Nov.) 1939.

<sup>98</sup> Minton, J. *Proc Roy Soc Med* **30** 285 (Jan.) 1937, abstracted, *Arch Ophth* **17** 565 (March) 1937.

<sup>99</sup> Orr, H. C., and Young, J. H. *Brit M J* **1** 1119 (June 1) 1935.

<sup>100</sup> Tortella, L. P. *Arch de oftal hispano-am* **34** 544 (Oct.) 1934.



gitis The condition has followed prophylactic vaccination against rabies <sup>101</sup> and has occurred after combined inoculations against typhoid, cholera and dysentery <sup>102</sup> Bucy <sup>103</sup> reported a case in which sulfanilamide was the etiologic agent I have heard of a similar case and have seen a case of bilateral optic neuritis accompanied with unilateral paralysis of the sixth nerve in a boy of 7 who received sulfapyridine Kahoun <sup>104</sup> reported a case of optic neuritis due to carbon monoxide poisoning, I <sup>105</sup> reported a case in which retrobulbar neuritis and multiple sclerosis occurred in a healthy donor who gave 500 cc of blood twice within forty-eight hours, and both Moore <sup>84</sup> and Knapp <sup>106</sup> have discussed the occurrence of similar cases following severe hemorrhage

In many cases optic and retrobulbar neuritis are attributed to sinusitis A brief survey of the literature revealed 16 authors in favor of and 11 opposed to the theory of a sinus origin for these conditions Three investigators, Bedell,<sup>107</sup> Campbell <sup>108</sup> and Hoople,<sup>109</sup> Neuritis, Arch Ophth **16** 236 (Aug) 1936 favored operation only if there was a purulent sinusitis Moore <sup>84</sup> was opposed to the theory of a sinus origin, and Benedict <sup>85</sup> expressed the belief that operations on the sinuses act nonspecifically My opinion agrees with that of the five authorities cited

Carroll <sup>110</sup> recently stated "When a cure has been discovered for multiple sclerosis, a cure will have been found for retrobulbar neuritis in many cases" One can say with fully as much logic that when a cure has been discovered for retrobulbar neuritis a cure will have been found for multiple sclerosis in many cases I believe that symptoms of the latter referable to the spinal cord and those of involvement of the optic nerve are due to a pathologic process of the same type The location of the lesion determines the symptoms and signs of this

101 Cormack, H S, and Anderson, L A P Brit J Ophth **18** 167 (March) 1934 Hasabe Acta Soc ophth jap **38** 102 (July) 1934 Suzuki Ibid **39** 219, 1936

102 Shannon, C E G Bitemporal Paracentral Scotoma, Arch Ophth **6** 544 (October) 1931

103 Bucy, P C Toxic Optic Neuritis Resulting from Sulfanilamide, J A M A **109** 1007 (Sept 25) 1937

104 Kahoun, S Ceskoslov oftal **3** 122, 1937, abstracted, Am J Ophth **21** 340 (March) 1938

105 Duggan, W F Use of Vasodilators in Treatment of Retrobulbar Neuritis, Arch Ophth **16** 380 (Sept) 1936

106 Knapp, A Medical Ophthalmology, Philadelphia, P Blakiston's Son & Co, 1918, pp 407-409

107 Bedell, A New York State J Med **33** 361 (March 15) 1933

108 Campbell, E H Relationship of Sinusitis to Optic and Retrobulbar

109 Hoople, G D New York State J Med **33** 365 (March 15) 1933

110 Carroll, F D Retrobulbar Neuritis Observations on One Hundred Cases, Arch Ophth **24** 44 (July) 1940

disease It is probably for this reason that Traquair<sup>111</sup> stated that acute retrobulbar neuritis can be considered a monosymptomatic form of multiple sclerosis

The pathology of retrobulbar neuritis is the pathology of multiple sclerosis The pathology of the acute form is presumably the same as the pathology of neuromyelitis optica, first described as a clinical entity by Albutt Briefly, the optic nerves and other parts of the nervous system show localized areas of softening and necrosis with perivascular infiltration Ricker would call this stage peristasis, or leukostasis In cases of the healed form there are sclerotic plaques of glial origin around arterioles whose walls are thickened Demyelination is a characteristic change In some instances the arteriolar lumen is obliterated This is essentially an infarct Many observers in the past have stated that the glial cells grew and compressed the arterioles and the nerve fibers Actually, I believe that local circulatory failure causes the myelin to break down and that the glial overgrowth is secondary, not primary

Many years ago Dawson (quoted by Moore<sup>84</sup>) noted that the sites of predilection for disseminated sclerosis were related to (1) the terminal ramifications of end arteries and (2) areas where much glial tissue is normally present, as in the optic chiasm Moreover, Kennedy<sup>87</sup> has said that "the recent plaques in the rare autopsies of acute cases [of multiple sclerosis] are not sclerotic, they are infiltrations by fluid of the nerve tissue surrounding blood vessels" Kennedy stated the belief that the episodes, intermissions and curability of the acute crises of disseminated sclerosis "resemble the happenings of localized allergic edemas"

There must be a factor common to all cases of acute retrobulbar neuritis In analyzing the etiologic factors, it is obvious that in the case of carbon monoxide poisoning the retrobulbar neuritis was due to histotoxic anoxia, caused by loss of ability of the hemoglobin to transport sufficient oxygen to nourish the tissues The cases following hemorrhage can be ascribed to anemic anoxia However, when the retina, rather than the optic nerve, is the site of the lesion, one sees not ischemia but edema of the retina with narrowing of one or more of the branches of the central retinal artery Presumably, the same type of lesion is present in the optic nerve These lesions can be ascribed to overaction of homeostatic mechanisms which occur after hemorrhage It is known that after hemorrhage there is a generalized arteriolar constriction, due either to the action of the sympathetic nervous system or to release of epinephrine into the circulating blood or to both factors This reduces the capacity of the vascular system

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<sup>111</sup> Traquair, H M Tr Ophth Soc U Kingdom 50 351, 1930

If this compensatory arteriolar constriction results in excessive spasm, the reactions shift from the zone of normal to that of pathologic physiology. Moon<sup>26</sup> noted that excessive and prolonged arteriolar constriction, such as that produced by overdoses of epinephrine, can produce changes in capillary permeability by so limiting the access of blood to the capillaries that both they and the tissues supplied by them suffer from anoxia. In other words, if posthemorrhagic amaurosis is due to a "toxin," the "toxin" is epinephrine, and it causes amblyopia either of retinal or of retrobulbar origin because of a homeostatic mechanism which is physiologic in nature but pathologic in degree. Also, Landis has frequently reported that lack of oxygen is the most potent factor in causing increased capillary permeability.

In the rare cases of retrobulbar neuritis due to carbon monoxide poisoning and to hemorrhage anoxemia is present. In most of the cases of acute retrobulbar neuritis there is no anoxemia, but I believe that localized anoxia, due to dysfunction of one or two arteriolar capillary units, exists. This dysfunction manifests itself as arteriolar constriction with secondary increased capillary permeability, due to the anoxia resulting from the arteriolar spasm. Allergy, histamine, epinephrine and overaction of the sympathetic nervous system can all cause these arteriolar-capillary changes.

The idea that acute retrobulbar neuritis might be of vascular origin is not new. In 1931 Cross<sup>112</sup> stated that he "thought it possible that some cases of retro-ocular neuritis might be due to a spasm of small vessels going to the nerve-fibres, while others were due to small emboli. Some might be due to slight œdema, and others to slight thrombosis." Others who favored the vascular theory include Sourdille,<sup>113</sup> Schieck,<sup>114</sup> Aubaret and Sedan,<sup>115</sup> Snell,<sup>116</sup> Kennedy<sup>87</sup> and Bedell.<sup>117</sup>

In 1931 de Saint Martin<sup>118</sup> reported a case of retrobulbar neuritis occurring post partum in which improvement followed intramuscular injections of acetylcholine, and in 1934 Hartmann and Parfonry<sup>119</sup> reported a case of posthemorrhagic amblyopia in which improvement was obtained with acetylcholine after repeated transfusions had been of no avail. (Treatment for the anoxemia with transfusions did not help

112 Cross, R. *Tr Ophth Soc U Kingdom* **33** 43, 1913

113 Sourdille C. *Clin ophth* **6** 280, 1900, abstracted, *Arch Ophth* **30** 191, 1901

114 Schieck, F. *Arch f Ophth* **71** 466, 1909

115 Aubaret, E, and Sedan, L. *Clin opht* **17** 255, 1928

116 Snell, A. *New York State J Med* **33** 370 (March 15) 1933

117 Bedell, A. *New York State J Med* **36** 959 (July 1) 1936

118 de Saint-Martin. *Ann d'ocul* **168** 102 (Feb) 1931

119 Hartmann, E, and Parfonry, J. *Bull Soc d'opht de Paris*, February 1934, p 56

the localized tissue anoxia ) These authors stated that vascular spasm was the cause of the amaurosis

I<sup>120</sup> recently reported the results of vasodilator therapy in 23 patients who had 27 attacks of acute retrobulbar neuritis Twenty-nine eyes were involved There were 9 males and 14 females in the series No sinuses were opened, no teeth were removed, no vaccines were used, and no foreign protein therapy was employed in any case

In 18 attacks the average treatment consisted in eight daily intravenous injections of 0.1 Gm of sodium nitrite In 4 attacks from three to nine intramuscular injections of acetylcholine bromide (0.1 Gm ) were used In 1 attack three daily inhalations of amyl nitrite was the only therapy employed In the other 4 attacks various combinations of the aforementioned drugs were used

Before treatment, 17 eyes (58.6 per cent) had vision ranging from perception of hand movements to 20/100, after treatment, 25 eyes (86.2 per cent) had vision of from 20/30 to 20/15 In no instance did vision become worse with treatment, but in 4 eyes the final vision was less than 20/200 For the 25 eyes in which vision improved the average duration of loss of sight prior to treatment was 16 days and the average time required for the attainment of the best final vision was 97 days Papilledema and multiple sclerosis were not of unfavorable prognostic significance The earlier that treatment was instituted, the better were the final visual results For this reason, I stated that valuable time should not be wasted in searching for foci of infection or other questionable etiologic factors before starting vasodilator therapy

Of the last 11 attacks in which treatment was given a definite history of exposure to cold or to a sudden change in climatic conditions was obtained in 9 The change was usually from warm to cold weather or from a cold dry to a cold wet atmosphere Such changes often occur even in the warmer months of the year For example, May 1938 was a relatively cold month, May 28 was stormy and May 29 was very cold Four attacks were seen in this particular month, and 3 of them occurred between May 26 and May 30

In 1 case exposure to cold seemed to be the precipitating factor The patient, a woman of 23, had walked against a stiff, cold wind on Feb 22, 1939 The next day, on awakening, she discovered that vision in the left eye was much reduced, that afternoon vision failed in the right eye On February 24 vision was found to be 4/200 in the right eye and was limited to perception of hand movements in the left eye She received two intramuscular injections of sodium nitrite and three inhalations of amyl nitrite and then disappeared from the clinic Information was received from another clinic that on March 7 vision was 20/20 in the right eye and 4/200 in the left eye After that date she failed to return

<sup>120</sup> Duggan, W. F. Acute Retrobulbar Neuritis as a Manifestation of Acute Localized Tissue Anoxia, *Arch Ophth* 25:299 (Feb) 1941

to the second clinic (I have recently seen 2 similar cases in which exposure to cold was the only possible etiologic factor. In both cases vision was 20/16 in each eye after vasodilator therapy.)

In this case the reaction was attributed to histamine, formed in the skin and carried to the vessels of the optic nerve by the blood. Horton, Brown and Roth<sup>68</sup> reported an analogous case in which a man collapsed and was unconscious for forty minutes after running about  $\frac{1}{5}$  mile (320 meters) against a stiff wind at a temperature of 30 F below zero. The patient did not recover his strength for a week. Had my patient also been unable to walk or had the patient of Horton and associates lost his vision, the diagnosis of neuromyelitis optica could have been made. In other words, the distribution, number and location of lesions determine whether unilateral or bilateral retrobulbar neuritis, myelitis or neuromyelitis optica develops. The differences are those of degree, rather than of kind.

Edwards<sup>121</sup> reported an interesting case of acute retrobulbar neuritis in a woman of 37. Vision in one eye was 4/200, owing to a previous attack of acute retrobulbar neuritis. When her remaining eye was involved, eighteen months later, Edwards used vasodilators, transfusions of blood and inhalations of 100 per cent oxygen. After three weeks her vision had improved to 20/40, a small scotoma was still present. All therapy was directed toward relief of the vascular spasm and tissue anoxia.

Ravin<sup>122</sup> reported 5 cases of optic neuritis in which the drug of choice was erythrityl tetranitrate, a vasodilator, which was given orally. He also gave the patient thiamine hydrochloride, not to relieve a hypothetical vitamin B<sub>1</sub> deficiency but because it acts indirectly as a vasodilator. Visual acuities as determined on several occasions before treatment were 20/70, perception of hand movements, 20/30, 20/70 and 20/200, respectively, after treatment the final visual acuities were 20/30, 20/20, 20/30 +, 20/20 and 20/30, respectively, on several occasions. Ravin's report is of interest because he desired to treat the patients orally rather than intravenously. I can corroborate his results, because I have found that the oral administration of erythrityl tetranitrate and nicotinic acid are useful both when used alone and as an adjunct to intravenous injection of sodium nitrite.

Finally, Cordes<sup>123</sup> reported a case of acute retrobulbar neuritis in which vision improved from 2/200 to 20/20 in eight days with vasodilator therapy and a case of optic neuritis in which vision improved from light perception to 20/20 in four weeks with subcutaneous injections of 100 mg of sodium nitrite.

121 Edwards, D. L. *J. Oklahoma M. A.* **34** 201 (May) 1941

122 Ravin, L. C. *Am. J. Ophth.* **26** 188 (Feb) 1943

123 Cordes, F. C. *Am. J. Ophth.* **26** 916 (Sept) 1943

To sum up, acute retrobulbar neuritis is an acute vascular catastrophe occurring in the optic nerve, chiasm or tract, resulting in edema and leading to tissue anoxia and loss of function. Increased capillary permeability, which may be primary, but is probably secondary to arteriolar spasm in most cases, is the basic pathologic process in all cases of this condition. Tissue anoxia occurs because of this capillary change. This pathology is the pathology of allergy, histamine poisoning and shock. The arteriolar-capillary changes are the final common pathway for a number of etiologic agents, which can act on the arterioles or the capillaries or both. Overaction or underaction of certain homeostatic mechanisms explains the condition in many cases. In many cases the disturbance is related to exposure to cold or to a sudden change in the weather. This relationship is causal, rather than casual. On clinical evidence histamine is probably the etiologic agent in these cases. A histamine origin also explains the cases of retrobulbar neuritis attributed to focal infection and to allergy.

#### UVEA

*Iris and Ciliary Body*—Kronfeld,<sup>124</sup> in discussing iritis and iridocyclitis, noted that there are ciliary injection, edema of the iris and exudate in the anterior chamber. The exudate may consist in (a) increased protein, (b) fibrin, (c) cells or (d) clumps of cells on the back of the cornea. Nodules may form, when these heal and are absorbed, atrophic areas remain.

According to Davids,<sup>125</sup> nodules which form in the eye may be due to specific or nonspecific factors. He found that nodules (or granulomas) were associated with sympathetic ophthalmia, rheumatic fever and herpetic iritis and pointed out that it is the common tendency to consider such nodules as indicating tuberculosis. Caution in diagnosis is indicated.

In cases of rheumatic uveitis, Marchesani<sup>126</sup> found changes in the uvea, sclera and retina characteristic of so-called rheumatic tissue damage. In the early stages the connective tissue showed fibrinoid swellings, later, nodules of cells developed, composed chiefly of large histiocytes with basophilic protoplasm, finally, the foci changed to connective tissue scars. Giant cells were often present. Unlike the lesions of true tuberculosis, these granulomas produce little tissue reaction, much formation of connective tissue and no caseation. Marchesani expressed the opinion that these changes of "rheumatic" origin represent an allergic-hyperergic inflammation.

<sup>124</sup> Kronfeld, P. Introduction to Ophthalmology, Springfield, Ill., Charles C. Thomas, Publisher, 1938.

<sup>125</sup> Davids, H. Nodule Formation in the Eye, Arch. Ophth. **23** 432 (Feb.) 1940.

<sup>126</sup> Marchesani, O. Rheumatic Uveitis, Arch. Ophth. **23** 431 (Feb.) 1940.

One animal experiment is worthy of report Spadavecchia<sup>127</sup> sensitized rabbits to horse serum After a suitable period he injected 10 cc intraperitoneally, followed by instillation of irritating chemicals into the conjunctival sac Severe iritis resulted Control experiments seemed to indicate that the reaction was specific Among the irritants used were chloroform and histamine While this was an animal experiment, and therefore not typical of clinical conditions, it may explain those cases of iritic "irritability" which follow trauma to the cornea In such cases the tears could be the source of the histamine, for Ridley<sup>70</sup> recently reported finding a histamine-like substance in normal tears Moreover, Ridley's histamine-like substance serves to explain the swollen lids which develop after weeping and which are often seen in cases of acute iritis and iridocyclitis when tearing is copious

The list of causes of iritis and iridocyclitis includes focal infection, allergy, herpes, syphilis, tuberculosis, endocrine imbalance, rheumatism, gout, antointoxication, acute infectious diseases, brucellosis and the common head cold Undoubtedly, these conditions have preceded or accompanied anterior uveitis, but is the relationship necessarily one of cause and effect? The ocular changes may be the same as those occurring in the other tissues of the body in these clinically different diseases All these alleged causes have one thing in common—vascular dysfunction, whether due to histamine, a histamine-like effect associated with allergy or a failure of arteriolar and capillary homeostasis Moreover, these causes are the alleged causes of every other ocular manifestation of allergy discussed thus far in this essay

In a recent article I<sup>128</sup> compared acute iritis and iridocyclitis with acute retrobulbar neuritis, acute exudative choroiditis and acute spastic closure of the central retinal artery In these superficially different lesions the early pathologic changes can be attributed to arteriolar spasm, increased capillary dilatation and permeability and transudation of plasma and white cells into the perivascular tissues The superficial differences in these various lesions depend on the anatomic character of the affected tissues Early changes are due to capillary anoxia, which causes tissue anoxia Acute focal necroses may result, in healing these are replaced by scar tissue or atrophic areas or a combination of the two

With acute retrobulbar neuritis there are localized edema and round cell infiltration in the optic nerve Because of the sheath of the nerve pressure may be exerted on all the fibers in the optic nerve, leading in some instances to total blindness Yet after healing occurs, only a small bundle of fibers may be permanently affected This bundle

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127 Spadavecchia, V *Ann. di ottal e clin ocul* **66** 241 (April) 1938

128 Duggan, W F *Vascular Basis of Uveal Disease*, Arch Ophth **24** 1123 (Dec) 1940

(as shown by scotometry) consists of the fibers supplied by the spastic arteriole, which is often obliterated

With acute exudative chorioiditis the lesion is subretinal, the edema is pronounced and the retina is secondarily affected. Complete anoxia accounts for the atrophy, while partial or relative anoxia at the edges of the lesion is probably the stimulus for proliferation of retinal pigment there

With spastic closure of the central retinal artery or one of its branches the spasm is visible, the edema is obvious and the area of edema also corresponds to the area of retina supplied by the involved artery. The loss of function in the field also corresponds to the location and amount of vascular change

With acute iritis and iridocyclitis there is edema of the iris and the aqueous (prestasis), with peristasis, the cells, which account for the perivascular infiltration in the preceding conditions, pass out into the aqueous because of the loose and spongy nature of the anterior uveal tissue. If the arteriolar spasm is moderate, nodules may form, if severe, focal areas of necrosis occur

After pointing out that iritis, iridocyclitis, sympathetic ophthalmia and Harada's disease (involvement of the iris, ciliary body, choroid and optic nerve) show only quantitative variations in the extent and severity of the lesions, I reported 11 cases of iritis and iridocyclitis (10 of the acute and 1 of the subacute form) in which only vasodilator therapy was used (Sodium nitrite was given intravenously and erythrityl tetranitrate by mouth). The time required for clinical cure was between five and fifteen days, the average time was nine days per case. Minimal amounts of mydriatics were used, and no patient was hospitalized or even told to remain away from work

Two of the patients with acute iridocyclitis had syphilis, 1 was receiving antisyphilitic treatment, the other was not. These patients were completely cured in five and nine days, respectively

I also described a case of postoperative iridocyclitis which followed an uncomplicated cataract operation. The condition could have been diagnosed either as early sympathetic ophthalmia or as endophthalmitis phacoanaphylactica. Injections of milk, use of salicylates and frequent instillations of atropine were without effect. Four weeks after operation the patient received four intravenous injections of sodium nitrite and oral doses of erythrityl tetranitrate (15 mg) twice daily by mouth. After ten days the eye was white and the tension, which had been low, was normal

In my conclusions, I stated that the striking and rapid improvement which followed vasodilator therapy in these cases was of fundamental biologic importance. I suggested histamine as a "likely etiologic agent because (1) histamine constricts arterioles and both dilates and increases



the permeability of capillaries, (2) histamine can account for cases ascribed to allergy, focal infection and cold, and (3) histamine is set free when tissue is traumatized "

Arkhangelskiy<sup>129</sup> stated nine years ago that postoperative cyclitis was due to mechanical irritation of the ciliary nerves and that a neuro-humoral factor must be considered in any theory concerned with the causation and development of this lesion. He did not mention antidromic impulses or axon reflexes or imply that histamine might be the neurohumoral agent, but he expressed the opinion that dental infection was also a factor of importance.

Kennedy, Wortis and Wortis,<sup>89</sup> after mentioning that it is commonly known that vascular accidents occur in the brain in the course of an untreated syphilitic infection, stated

The very fact that many of these episodes are rapid to occur and clear up without treatment is evidence in favor of the possibility of angiospasm being the causative mechanism.

What is true for the brain should be true for the eye. In cases of untreated infections the iritis may be of reflex origin, in cases in which treatment is employed it may be an anaphylactoid reaction. In either case its origin is vascular.

During the past two years I have treated 6 additional patients with acute iritis and iridocyclitis with vasodilators alone. In 1 of these patients the condition followed a cataract operation. All patients were clinically cured in from four to seven days. No teeth were extracted, no salicylates were given, no foreign protein therapy was instituted, and minimal amounts of atropine or scopolamine were used. The results were uniformly good, and the patients were spared the loss of time from work, the expense of hospitalization and the discomfort and malaise which often accompany "shock" therapy.

In conclusion, it may be stated that acute iritis and iridocyclitis are manifestations of vascular dysfunction. The clinicopathologic changes represent varying degrees of prestasis, or liquor stasis, and peristasis, or leukostasis, which are due to increased capillary permeability. These capillary changes may be primary, or, what is more likely, because of the favorable response of these conditions to vasodilator therapy, they are secondary to arteriolar spasm. The pathology is that of allergy, of histamine poisoning and of epinephrine poisoning. Not all cases have the same cause, but in all cases the origin is vascular. Vasodilators act by ensuring an adequate supply of oxygen-containing blood to the capillaries and tissues, thereby relieving capillary and tissue anoxia.

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<sup>129</sup> Arkhangelskiy, V. N. *Sovet vestnik oftal* 8 10, 1936, abstracted, *Arch Ophth* 16 712 (Oct) 1936.

In all cases the condition may be considered as of allergic origin, but such a conception must be broadened to include forms due to physical allergy, to histamine and to overaction of the sympathetic nervous system. The focal nature of the lesions must be due to hypersensitivity of one or more arteriolar-capillary units in the anterior part of the uvea. This hypersensitivity of terminal units explains only why iritis develops in some cases, iridocyclitis in others and choroiditis in still others. There is a definite age incidence for these lesions, which may be due in part to endocrine influences, relative avitaminosis or imbalance of the autonomic nervous system. The vascular changes are the final common pathway for a number of etiologic factors. In most cases there are probably multiple causes, no one of which by itself could produce acute iritis or iridocyclitis but which, acting together, shift the reactions in the tissues from the zone of normal physiology into the zone of pathology.

*Acute Exudative Choroiditis*—Many years ago, Moore<sup>84</sup> asserted that acute choroiditis was similar in many respects to embolism of the central retinal artery or one of its branches. He stated that such a hypothesis was more plausible than attributing the lesions to tuberculosis. In 1925 closure of the retinal artery was attributed to emboli in most cases. With increasing knowledge of vascular physiology, the tendency is usually to attribute the condition to spasm. It is not unlikely that today Moore would alter his statement and attribute acute exudative choroiditis to spasm of the choroidal arteries rather than to embolism.

In 1939 Heath<sup>130</sup> mentioned the lack of evidence supporting tuberculosis as a cause of acute choroiditis, the absence of even questionable foci of infection in many cases and the presence of spasm of retinal arteries in 4 of his 24 cases. Among the conditions credited with causing acute choroiditis are chilling, pregnancy, lactation, influenza, intestinal infection, head colds, focal infection, multiple sclerosis and allergy. The etiologic factors are strikingly similar to the causes of acute retrobulbar neuritis, acute iritis and even closure of the central retinal artery. Heath also stated that "the frequent and severe involvement of the vessels has led many to suppose that the condition is primarily vascular." He personally did not favor this theory.

Recently I<sup>131</sup> reported 5 cases of acute exudative choroiditis (3 cases were of the juxtapapillary type) in which I used only vasodilator therapy. I gave twelve to fourteen intravenous injections of sodium nitrite and erythrityl tetranitrate by mouth. One patient, who was not materially improved, also had closure of the inferior division of the central retinal artery. Before treatment the other 4 patients had vision

<sup>130</sup> Heath, C. Brit J Ophth **23** 289 (May) 1939

<sup>131</sup> Duggan, W. F. Acute Exudative Choroiditis, Arch Ophth **23** 930 (May) 1940

of 20/30 —, 8/200, 20/100 and 20/100, respectively. After treatment the final visual acuity and the time required for cure were 20/20 — (nine days), 20/40 — (twenty-one days), 20/20 — (nineteen days) and 20/30 — (nine days), respectively. The patient attaining vision of 20/40 — was not seen again for six weeks, at which time vision was 20/20. The patient who attained visual acuity of 20/30 — had had vision of 20/30 for a year preceding the attack because of two previous attacks. In these 4 patients the lesions in the fundus subsided completely in fourteen, twenty-one, nineteen and twenty-nine days, respectively.

Cordes<sup>123</sup> reported equally good results in 2 patients who were treated similarly.

I commented on the basic similarity of this lesion, acute retrobulbar neuritis and acute spastic closure of the central retinal artery. All three conditions are manifestations of tissue anoxia resulting from arteriolar spasm and increased capillary permeability. I suggested histamine as a possible etiologic factor because this could explain the cases occurring in cold weather as well as those attributed to focal infection. I also noted that the pathologic changes of histamine poisoning and those resulting from overdoses of epinephrine were similar and that both substances produced lesions by causing varying degrees of prestasis, peristasis and stasis.

The pathology of acute choroiditis is the pathology of allergy, and both are manifestations of a disturbance of vascular physiology. For this reason I said "the use of vasodilators for the treatment of this condition has a sound physiologic and pathologic basis."

*Choroidosis Serosa Centralis*—There is a condition called serous retinopathy by Duke-Elder<sup>132</sup> which has been variously attributed to allergy, focal infection and "toxemia." Some authors believe it to arise from retinal angiospasm. Among the diagnoses offered by this group are retinitis centralis (Asayama), central angiospastic retinitis (Horniker), central angiospastic retinopathy (Gifford and Marquardt), retinal capillarosis (Cattaneo), angioneurotic macular degeneration (Candian) and juvenile exudative macular retinitis (Junius). Cattaneo<sup>133</sup> stated that the lesions may be macular, paramacular or disseminated, and he expressed the belief that circinate retinitis, senile macular exudative retinitis and disciform degeneration of the macula are also due to retinal angiopathy.

Another group of observers (Masada, Batten, Oguchi, Abe and Riehm) have described similar lesions but attributed them to subretinal

132 Duke-Elder, W. S. *Textbook of Ophthalmology*, St. Louis, C. V. Mosby Company, 1941, vol. 3, pp. 2592-2594.

133 Cattaneo, D. *Ann di ottal e clin ocul* 65 721 (Oct.) 1937.

edema originating from the choriocapillaris Walsh and Sloan<sup>134</sup> reviewed this aspect of the subject fully in 1936 They pointed out that moderate diminution of central vision, a positive scotoma, micropsia and, usually, transitory hyperopia were the important signs and symptoms In general, the scotoma was larger for blue than for red, indicating a lesion interfering with the function of the rods and cones They offered the term "idiopathic flat detachment of the macula" to describe the condition, and they suggested that focal infection or a circulatory disturbance, either angioneurotic or allergic in origin, must be considered as an etiologic factor

The advisability of including cases of disciform degeneration of the macula in this group is based on Cattaneo's opinion and on a recent article by Verhoeff and Grossman,<sup>135</sup> who described 3 cases and reviewed the literature For 1 of their cases they stated "the possibility cannot be excluded that the blood was derived from the choriocapillaris by diapedesis", and for another case they said "there was a serous exudate occurring primarily beneath the pigment epithelium and elevating the retina here in the form of a mound" Later, they said "the observations in our cases do not exclude the possibility of a localized vascular lesion" Verhoeff and Grossman<sup>136</sup> closed the discussion of their article with the following words

a typical lesion is due to organization of a hemorrhagic extravasation which is primarily beneath the pigment epithelium In some cases the hemorrhage may be due to urticaria I can even bring my favorite factor, allergy, into the question

It is difficult to differentiate lesions due to choroidal angiopathy from those due to retinal angiopathy They have the same etiologic background However, this differentiation can be made by scotometry In the cases of choroidal origin there is always a scotoma which is as large for a blue test object as for a red test object of the same size, or even larger Micropsia and transitory hyperopia occur in the cases with but slight depression of the visual acuity, and elevation of the macular region (up to 3 or 4 D in some cases) is always present The retinal alterations (white spots, pigmentation or depigmentation) are the most obvious, but the least important, changes in the fundus

In my opinion, these subretinal lesions bear the same relation to acute exudative choroiditis as an urticarial wheal bears to erythema nodosum These lesions represent prestasis, or liquor stasis, while acute exudative choroiditis and erythema nodosum represent varying

<sup>134</sup> Walsh, F B, and Sloan, L L Am J Ophth **19** 195 (March) 1936

<sup>135</sup> Verhoeff, F H, and Grossman, H P Pathogenesis of Disciform Degeneration of the Macula Arch Ophth **18** 561 (Oct) 1937

<sup>136</sup> Verhoeff, F H and Grossman, H P Pathogenesis of Disciform Degeneration of the Macula, Arch Ophth **19** 467 (March) 1938

degrees of peristasis and stasis, the vascular catastrophe is so severe that focal necroses occur in the latter conditions

I<sup>137</sup> reported 13 cases of central subretinal edema. I prefer the term "choroidosis serosa centralis" to designate this condition due to choroidal angiopathy. In all cases it was considered to be a manifestation of localized capillary and tissue anoxia and may be interpreted as due to allergy because the lesion is fundamentally a wheal. Vasodilators were used to increase the supply of oxygen-containing blood to the tissues involved. An analysis of these cases is of interest.

In the cases (7) of less severe central subretinal edema there was only a central scotoma for blue and, in some instances, a scotoma for a 1 mm white test object at 1,000 mm. Visual acuity varied from 20/50 to 20/30 before treatment, after treatment, it varied from 20/30 to 20/15. The macular region was elevated from 1 to 2 D before treatment. The swelling subsided with improvement in vision. Complete cure required from five to twenty-one days (average, ten days).

Three other cases were typical instances of early disciform degeneration of the macula. In the first, a woman of 48 had vision of 20/100, with intravenous injections of sodium nitrite vision improved to 20/30 in sixteen days. In the second, a man of 61 had vision of 20/30—; with treatment it improved to 20/20— in one week. This was maintained for one month, after which the vision suddenly decreased to 12/200, owing to a large subretinal hemorrhage. In the third case a woman of 65 had vision of 20/100, this improved with vasodilator therapy to 20/50 in thirteen days and was maintained for three months. After this the patient failed to return for further observation. One other patient, a man of 56, whose vision had been poor for four or five years, had a condition suggestive of disciform degeneration of the macula. Vision was 20/200 in each eye, the macular regions were elevated from 2 to 3 D, and there was a central scotoma for white and blue, the scotoma for red was smaller than the scotoma for blue. After twenty-three intravenous injections of sodium nitrite (0.1 Gm.), in ten weeks vision improved to 20/50— and 20/70—, the scotomas decreased in size and density, and the macular elevation had decreased to about 1 D.

Many of the 13 patients gave a history of other allergic lesions. One patient had had two attacks of acute retrobulbar neuritis, both attacks cleared in a few days with the same vasodilator therapy. Another patient had had bilateral retrobulbar neuritis thirty years earlier, with permanent field defects and some atrophy of the optic nerve. As his fields had been plotted prior to the attack of choroiditis serosa centralis, it was easy to diagnose the presence of the new submacular

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137 Duggan, W. F. Choroidosis Centralis Serosa, Arch Ophth 27 123 (Jan) 1942

lesion (I have recently seen another patient who had both lesions) One patient had lost useful vision in her other eye twelve years before the present attack, after acute exudative choroiditis at the macula. Another patient suffered from attacks of urticaria. In 1 patient the subretinal lesion developed fourteen hours after an intravenous injection of sodium iodide and sodium salicylate. Finally, a girl of 20 had onset of both central subretinal edema and Bell's palsy on the same side after walking 1 mile (1.6 kilometers) to work on Jan 22, 1940, when the outdoor temperature was 28 F. With intravenous injections of sodium nitrite, the ocular lesion cleared in eight days and Bell's palsy in eleven days. The disturbance in this case could well have been due to hypersensitiveness to cold and therefore could be attributed to histamine, formed in the skin and then carried by the blood to the arterioles and capillaries in the choroid and in the facial nerve.

Cordes<sup>123</sup> reported a similar case of a woman aged 34. Her vision improved from 20/200 to 20/20 in one week with daily subcutaneous injections of sodium nitrite and three daily small doses of typhoid vaccine given intravenously.

Horniker,<sup>138</sup> who used the term central angiospastic retinitis, expressed the belief that exposure to cold was a causative factor in some of these cases and that vasodilators were of value.

Gifford and Marquardt<sup>139</sup> stated preference for the term "central angiospastic retinopathy." They used antispasmodic treatment with benefit in their 8 cases. They also expressed the belief that exposure to cold should be avoided by patients with this lesion.

In a later article, Gifford<sup>140</sup> reported on 23 additional cases of central angiospastic retinopathy (choroidosis centralis serosa?). He stated that peripheral angiospasm is the cause of these macular lesions and that protection against cold and abstinence from tobacco are indicated for patients with such a condition. His treatment included administration of papaverine intravenously, typhoid vaccine intravenously; phenobarbital, a preparation of theobromine and phenobarbital (Theominal) or a deproteinized pancreatic extract (Depropanex) intramuscularly, nicotinic acid or the vitamin B complex, sodium nitrite by vein, neostigmine by mouth, thyroid extract in cases of lowered basal metabolism, and a regimen including plenty of rest and avoidance of fatigue and nervous strain when it seemed practical. No patient

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<sup>138</sup> Horniker, E. *Ann di ottal e clin ocul* **55** 55, 1927, *Arch f Ophth.* **123** 286, 1929, *Klin Monatsbl f Augenh* **98** 487, 1937.

<sup>139</sup> Gifford, S. R., and Marquardt, G. Central Angiospastic Retinopathy. *Arch Ophth* **21** 211 (Feb) 1939.

<sup>140</sup> Gifford, S. R. Evaluation of Ocular Angiospasm, *Arch Ophth* **31** 453 (June) 1944.

received all the aforementioned antispasmodics, but most of them received various combinations of them

Cordes<sup>141</sup> has also reported on a type of foveomacular retinitis observed in the United States Navy. Approximately 176 cases were studied in detail, but many more cases were seen. Clinically, this retinitis resembled Duke-Elder's central serous retinopathy or Gifford's central angiospastic retinopathy. Vasomotor instability, emotional upsets, fear, worry, anger and the excessive use of tobacco, all of which, either alone or in various combinations, can, and often do, produce angiospasm, were mentioned by Cordes in his discussion of the etiology of this lesion. He concluded that the etiologic factors deserved further study, with special consideration to peripheral vascular disease and angiospasm, and that the use of vasodilators in the early stages seemed beneficial.

Finally, Bothman,<sup>142</sup> after abstracting a case of central edema with blurring which was reported by Binckerhoff and in which normal vision was regained after treatment with vasodilators and typhoid vaccine, said, "We believe that this type of lesion is due to allergy."

I believe that choroidosis serosa centralis is often a manifestation of allergy and that disciform degeneration, which occurs in the older patients, differs only in degree from this condition in young people. Both are manifestations of tissue anoxia. Vascular dysfunction causes the tissue anoxia, and allergy is often the cause of the vascular dysfunction. The use of vasodilators in this condition is based on the pathologic physiology of the lesion.

#### SCLERA

The nonpyogenic scleral "inflammations," which Duke-Elder<sup>143</sup> divided into episcleritis (nodular episcleritis and episcleritis periodica fugax) and scleritis (anterior, brawny and posterior scleritis, and sclerokeratitis) have been ascribed to gout, rheumatism, tuberculosis, syphilis, allergy, focal infection and menstruation. Regarding these conditions, Friedenwald<sup>144</sup> stated:

The etiology seems to be related to that of the non-specific inflammations of the iris, ciliary body and choroid. The histological picture presented by all of these cases consists of a necrosis of some of the scleral fibers with surrounding edema and round cell infiltration.

If the words "scleral fibers" are replaced by "nerve fibers," the description would apply to acute retrobulbar neuritis, multiple sclerosis or neuromyelitis optica.

141 Cordes, F. C. *Am J Ophth* **27** 803 (Aug.) 1944

142 Bothman, L. *The 1944 Year Book of the Eye, Ear, Nose and Throat*, Chicago: The Year Book Publishers, Inc., 1944, p. 149.

143 Duke-Elder,<sup>132</sup> 1938, vol. 2, pp. 2044-2069.

144 Friedenwald, J. S. *The Pathology of the Eye*, New York, The Macmillan Company, 1929, pp. 67-69.

Duke-Elder's description is more complete. He stated <sup>143</sup>

The lesion is characterized especially by the presence of mononuclear lymphocytes, tightly packed masses of which make up the bulk of the inflammatory nodules or the areas of diffuse swelling. In the superficial episcleral lesions the conjunctiva is infiltrated in its sub-epithelial layer, as well as the superficial parts of the sclera, the laminae of which are separated by oedema and surrounded by rows or spindle-shaped masses of lymphocytes. In these lesions extreme vascular engorgement and lymphatic dilatation occur almost invariably (Schumer, 1895, Uhthoff, 1900). In the deeper lesions the same infiltration occurs.

In the milder cases the inflammatory exudation may disappear leaving little or no trace, but in most cases of any degree of severity necrosis of the cells and fibres results while the new vessels undergo an obliterating endarteritis, or alternately fatty or hyaline degeneration may ensue. The necrotic tissue is then slowly absorbed, and as a rule proliferation of new fibrous tissue replaces the atrophy, leaving a scar.

It must be apparent that the foregoing description is a description of allergy. The edema is due to increased capillary permeability, and the focal necroses are due to arteriolar spasm, which may also be the cause of the increased capillary permeability. This is borne out by the fact that in cases of severe scleritis there is obliteration of the arterioles, just as in case of healed acute choroiditis one or two narrowed or obliterated choroidal vessels can be seen in the floor of the lesion. However, this arteriolar lesion is primary rather than secondary, as is commonly believed.

Purtscher <sup>145</sup> recently reported the case of a man of 67 who had serous tenonitis of the left eye and extensive choroidal detachment. A few days later the right eye was similarly affected. Still later retinal detachment and hypotony developed. After six months the detachments and hypotony disappeared. Purtscher asserted that the serous tenonitis and choroidal detachment represented an edema which was secondary to posterior scleritis, the posterior scleritis was ascribed to a vasomotor neurosis on an allergic basis.

On the assumption that many of these scleral inflammations are manifestations of localized tissue anoxia due to varying degrees of arteriolar spasm and increased capillary permeability, whether the results of allergy, histamine or overaction of the sympathetic nervous system, treatment with vasodilators only was instituted in 5 cases (intravenous injections of 100 mg of sodium nitrite and administration of erythrityl tetranitrate by mouth). These cases, which have been reported in full elsewhere, <sup>146</sup> are summarized as follows.

CASE 1—W P, a man of 58, was seen on March 24, 1938, with episcleritis of the right eye. Symptoms had been present for six days. He received 30 mg of erythrityl tetranitrate twice daily for five days and sodium nitrite intra-

145 Purtscher, E. *Klin Monatsbl f Augenh* 94 12 (Jan), 141 (Feb) 1938

146 Duggan, W F. Role of Anoxia in the Production of Episcleritis and Scleritis. *Arch Ophth* 25 113 (Jan) 1941



venously on March 24 and 29. The nodule disappeared in two days, as did the symptoms. On the seventh day (March 31) only two dilated venules indicated the site of the former lesion. There was no immediate recurrence.

CASE 2—W. W., a man of 30, was seen on Aug. 13, 1938, with episcleritis of the right eye. Symptoms had been present for one month. He had had similar attacks in both eyes in the past. He received five daily injections of sodium nitrite and then took 15 mg. of erythrityl tetranitrate twice daily until August 21. On August 17 the right eye was free from symptoms and practically white. No recurrence took place during the next three weeks.

CASE 3—M. M., a man of 61, was seen on Sept. 30, 1938, with scleritis of the right eye, present for about nine days. Pain was an outstanding symptom. He received six daily injections of sodium nitrite, followed by administration of erythrityl tetranitrate by mouth for several days. Pain was relieved after the first injection, the tenderness disappeared after the fourth injection, and on October 7 the eye was almost completely white. He failed to return to the clinic for further observation.

CASE 4—Mrs. C. H., aged 68, was seen on Jan. 14, 1940 with moderately severe brawny scleritis of both eyes, which had been present in the right eye for two days and in the left eye for one day. The only ascertainable cause was exposure to cold weather, on January 11 and 12. She was immediately given an injection of sodium nitrite and 15 mg. of erythrityl tetranitrate by mouth in the evening. When she returned, at my request, on January 18, she was free from symptoms. There was only a tiny patch of episcleral congestion nasal to the limbus in each eye. A second injection of sodium nitrite was given. On January 22 both eyes were completely white.

CASE 5—I. S., a man of 65, was seen on Jan. 21, 1940 with episcleritis of the left eye, which had been present for about one week. The chemosis of the conjunctiva over the nodule was so intense that the conjunctiva protruded between the closed lids. His history was without significance except for exposure to cold on January 15. He received injections of sodium nitrite on January 21 and 22 and took 30 mg. of erythrityl tetranitrate for three nights. The chemosis had disappeared on January 22. On January 24 the eye appeared entirely white and normal. There have been no recurrences to date.

Vision was not affected in any of these cases. No therapy other than that mentioned was used in any case. Even mydriatics were not used except in examination of the fundi at the first visit of each patient. The time required for a clinical cure varied from three to eight days. This treatment is not empiric but is based on a consideration of the pathologic physiology in these cases. In all cases the inflammation could have been ascribed to allergy. In cases 4 and 5, in my opinion, however, the condition was due to exposure to cold and could be ascribed to histamine.

#### MISCELLANEOUS CONDITIONS

No mention has been made of the noninfectious inflammations of the lids and conjunctiva which occur after contact with drugs and cosmetics. While these are probably forms of drug allergy, the relation of cause and effect is obvious and a cure usually follows removal of the irritant.

Vernal conjunctivitis and trachoma are considered by many ophthalmologists to be manifestations of allergy. Inasmuch as I have had no opportunity to treat these conditions with vasodilators in order to discover whether or not they represent unusual types of localized tissue anoxia, I prefer not to burden the reader with a recapitulation of the literature.

For many years it has been known that cataract is occasionally associated with eczema, neurodermatitis and other lesions of the skin attributed to allergy. Daniel<sup>147</sup> discussed this in 1935. Since then, except for reports of cases, little of importance has appeared in the literature. Moreover, these cataracts must be treated surgically in the manner prescribed for other cataracts.

In many cases the onset of acute dacryocystitis may be due to allergic changes in the walls of the sac, similar to that occurring with vasomotor rhinitis (or noninfectious coryza, as it was called by a correspondent in the *British Medical Journal*). Secondary invasion of the edematous, ischemic walls of the sac by pyogenic organisms (Findlay<sup>18</sup>) usually necessitates surgical intervention.

Acute dacryoadenitis may also be allergic in the sense that there is intense edema of the gland, due to increased capillary permeability. Here, release of tension by opening the gland usually results in cure, just as a decompressing operation relieves acute glaucoma.

Migraine may be accompanied with spasm of the retinal artery, paralysis of ocular muscles and scotomas. It is considered to be due to spasm of cerebral arterioles, followed by development of a "wet" brain, due presumably to increased capillary permeability. The most effective types of therapy are those which (1) paralyze the sympathetic vasoconstrictors, (2) actively dilate arterioles or (3) supply pure oxygen (Alvarez). Whether migraine is due to allergy, endocrine influences or overaction of the sympathetic nervous system is still *sub judice*. In many cases migraine is probably of allergic origin. Vasodilator therapy seems to be of value.

#### NATURE OF VASCULAR SPASM

While there are many articles dealing with the role of vascular spasm in particular diseases or in single cases, the best presentation of the subject as a whole from the viewpoint of the experimental pathologist is Nedzel's<sup>148</sup> monograph.

According to Nedzel the activities of the autonomic nervous system, the endocrine glands and the chemical and metabolic processes of the body are intimately related. The demand of the cells for nutrition depends on environmental conditions and is controlled by the

<sup>147</sup> Daniel, R. K. Allergy and Cataracts, *J. A. M. A.* **105** 481 (Aug. 17) 1935.

<sup>148</sup> Nedzel, A. J. Vascular Spasm. Experimental Studies, Illinois Medical and Dental Monographs, Urbana, University of Illinois Press, 1943, vol. 3, nos. 3-4.

proper functioning of these three systems, whose changing behavior is reflected by the vascular system, particularly the peripheral circulation, since the capillaries are the medium through which oxygen and food-stuffs reach the cells and waste products are carried away

Therefore, it is reasonable to concentrate on the vascular system as the final regulator of the functions of the cell in its readjustments to the changing demands on its activities. The function of the vascular bed is to protect the organism from injurious exogenous and endogenous agents and to sustain normal life. Any inadequacies in the behavior of the terminal blood vessels will lead to impaired function, with resulting injury of particular groups of cells and the consequent production of disease.

In Nedzel's words

The transient variations in the resistance of the small blood vessels depend on the changes in tone of their walls. Hypertone and hypotone each [of] which may occur simultaneously in the whole body or in a large part of the body, interferes little with the passage of blood to the tissue, and hence does not impair the process of nutrition.

Another type of reaction is "vascular spasm." It is an exaggerated state of hypertone, and, what is more important, it is limited to a certain region, organ, or part of the body, or even to one artery. Spasm, in this sense, is always a localized phenomenon, a pathological occurrence, a diversion from the average amplitude and size of the normal ARS phase<sup>149</sup> of Petersen. The local phenomenon of vascular spasm means practically a complete stop, or a greatly diminished blood supply to the particular region, during a definite time interval, shorter or longer, but always exceeding the normal demand imposed by the environment.

vascular spasm is purely a functional phenomenon which is manifested by different pathological symptoms. Yet [spasm] if greatly pronounced or prolonged, or both, may precipitate disease in the organ or bodily region in which the disturbance is centered. This view has both clinical and experimental evidence to support it.

As the metabolism of the cell is dependent on oxygen, any appreciable diminution in available oxygen precludes normal cell function. For this reason, anoxic phenomena become increasingly important in studies of pathologic conditions of the human body, as well as in therapy.

The functional activity of the vascular bed appears to be of much significance in the development of many diseases, the etiology of which is attributed to other causes. Many different diseases themselves and different symptom-complexes can be explained on a vascular basis.

Basic disturbances—spasms in vascular beds—appeared [in animal experiments] in different regions and organs in varying degrees, thus leading to the formation of lesions in widely separated organs. These lesions are bases for different diseases, and yet their etiology is the same.

any factor which leads to vascular episodes in the body may cause one or another of several diseases, diseases which are very different clinically in their localization and manifestation.

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<sup>149</sup> ARS phase is a term used to denote the predominance of anabolism, reduction and vascular constriction (spasm).

While Nedzel did not discuss allergy as an entity, he did mention that some investigators have evoked allergy as the cause of acute rheumatic fever and of multiple sclerosis. He then went on to show that, according to his experiments and according to the work of other investigators, both these diseases are of vascular origin and that transitory periods of localized anoxia can account for the pathologic changes observed in these diseases. Throughout his presentation he repeatedly stated that sudden changes in the meteorologic environment constitute a common cause of anoxia due to vascular spasm and that persons with an unduly labile vascular system are the most susceptible. Undoubtedly, he would agree that these patients are allergic to their environment, that this is a variety of physical allergy, and that the basic lesion is arteriolar spasm and increased capillary permeability.

#### ALLERGY AND THE WEATHER

Petersen<sup>150</sup> a pathologist, has written extensively and logically about the relation of allergic manifestations to the weather. He used urticaria as an example and proved (in my opinion) that it is not necessary to assume that urticaria is always due to a specific antigen-antibody reaction. A few quotations may be of interest.

In discussing menstrual urticaria, he stated

Today we have taken over the same reasoning [that the bacterium is the whole story in etiology] and are searching deeply and frequently successfully for offending protein and other sensitizing agents. Again we disregard the constitutional—the conditioning factor of the individual patient. Personally, I doubt much the possibility of ever desensitizing in the true immunological sense.

Either we assume that we deal with an antigen that is constantly present, but with varying susceptibility and resistance on the part of the patient, or we must conclude that transient vasomotor alterations in the skin, incidental to and characteristic of this unstable type of individual, produce the lesions.

In a further chapter on the urticarias, he stated

Today, with the vogue of specific sensitization, we think only in terms of allergins, of antibody mechanisms [page 387].

We deal with more diseases of this type [urticaria] in America than in Europe merely because the environmental conditions are more severe and the opportunity for vascular instability becomes greater [page 388].

If one may assume that any aseptic lesion produced by increased capillary permeability, with or without a preceding arteriolar spasm, is basically an allergic lesion, then, as I have shown, acute glaucoma, iritis and iridocyclitis are manifestations of allergy in some cases, though not necessarily of allergy due to an antigen-antibody reaction. Petersen summarized 40 such cases and furnished the necessary meteorologic data. Every attack of acute glaucoma, iritis or iridocyclitis could be related to

<sup>150</sup> Petersen, W. F. The Patient and the Weather, Ann Arbor, Mich., Edwards Brothers, Inc., 1934, vol. 2, pp. 350-487.

a sudden alteration in the meteorologic environment, and the majority of them were referable to a polar infall (rising barometric pressure and falling temperature) It is the polar infall or passage of a cold front which is the cause of the "ARS" (anabolism, reduction, vascular spasm) phase in the body, and when this phase is present there is tissue anoxia of one or another organ or tissue or portion of a tissue. This localized anoxia, due to arteriolar spasm and increased capillary permeability, gives the localized picture of allergy It may well be that in the cases which can be related to weather changes one is dealing with an actual hypersensitivity or allergy to weather Certainly, the condition in these cases must be a variety of physical allergy

Petersen<sup>151</sup> also reported on the environmental changes (temperature, barometric pressure and rainfall) which occurred in some of the cases in which I employed vasodilator therapy, and which are referred to earlier in this article In the series of 13 cases which he studied, and which included instances of acute iritis, iridocyclitis, episcleritis, scleritis, choroiditis and retrobulbar neuritis, the onset in every case and the exacerbations in several cases were related in point of time to the passage of a polar air mass Petersen's comment was

any extreme in the environmental situation, whether toward cold or toward undue heat, is apt to find reflection in clinical symptoms for the simple reason that such changes entail major vasomotor adjustment While any one of many environmental factors may act as a precipitating force, the weather episode, on the background of season, is the most common of the energy impacts that are effective, for the biologic effect is apt to be prolonged The vascular spasm may exist for hours or even days, is subject to summation with repetition of environmental change and is, in addition, universal in its effectiveness in the population at large The meteorologic episode is universally effective, and the clinical reflection will be found in any organ or tissue

Mills<sup>152</sup> stated

Short cycle weather changes bring startling alterations in health and physiologic functions, alterations with which physicians should be thoroughly aware

I believe that man's reactions to the ever changing sea of air in which he lives constitute, in an unstable person, one of the major causes of disease and that allergy or, better, hypersensitivity or, still better, vasoneuropathy of physical origin (Urbach) is a pathologic reaction to a sudden change in this sea of air

#### COMMENT

Only eight years ago Pickworth,<sup>153</sup> in discussing the physiology and pathology of mental and emotional states, said

151 Petersen, W F Weather and Ocular Pathophysiology, Arch Ophth 29 747 (May) 1943

152 Mills, C Medical Climatology, Springfield, Ill, Charles C Thomas, Publisher, 1939

153 Pickworth, F A Brit M J 1 265 (Feb 5) 1938

Superstition demands an infinitely more complex control of the already complex nervous system, and thus hinders study of a humbler control by the vascular system

The clinical significance of regional vascular irregularities, however, needs many more years of further patient study

And Petersen,<sup>154</sup> in 1934, said

We are accustomed to regard the blood supply to the tissues as uniformly adequate unless gross pathological disturbances exist we seldom consider the possibility of regional or organ inadequacy of vascular function unless the clinical manifestations are obvious

As a matter of fact, variation in the oxygen supply to the tissues is probably one of the most common of events and dysfunction or inadequacy of the mechanism that has to do with oxygen supply is probably the fundamental cause of all disease

Poncher,<sup>155</sup> in a discussion of purpura, stated that the factors concerned with increased capillary permeability are hereditary, environmental, allergic, vasomotor endocrine and dietary influences and, finally, lack of oxygen

In my opinion, allergy of the ocular tissues may be considered an acute localized vascular catastrophe which is the result of arteriolar spasm or increased capillary permeability or both Tissue anoxia and loss of function are the immediate results

Capillary permeability is increased beyond physiologic limits by lack of available oxygen, by excessive arteriolar constriction and by histamine

Lack of available oxygen is often due to an anemic or histotoxic anoxemia, in which the blood is unable to carry adequate amounts of oxygen However, a physiologic anoxemia may occur in which, owing to an alkalosis (which may be due to primary carbon dioxide deficit, as in overbreathing, or to excessive intake of alkali), the dissociation curve of oxyhemoglobin is shifted to the left, so that the oxyhemoglobin does not dissociate normally in the capillaries but retains its attached oxygen A lowering of the temperature of whole blood also shifts the dissociation curve of oxyhemoglobin to the left

Arteriolar spasm may be caused by overaction of the sympathetic nervous system, by an excess of epinephrine in the circulating blood; by nicotine, by histamine or histamine-like substances, and by a decreased formation or an increased destruction of acetylcholine, the vasodilator hormone of the body

Even the vitamins may act via the capillaries and arterioles Lack of ascorbic acid increases capillary permeability Thiamine according to Minz,<sup>156</sup> acts by augmenting the action of acetylcholine, Spies, Bean

<sup>154</sup> Petersen,<sup>150</sup> p 11

<sup>155</sup> Poncher, H G Purpura as a Symptom in Pediatric Practice, J A M A **104** 1690 (May 11) 1935

<sup>156</sup> Minz, B Presse méd **76**•1406 (Sept 21) 1938

and Stone<sup>157</sup> and many others have reported that nicotinic acid dilates arterioles, and it is known that riboflavin is concerned with oxidative processes

Excess or deficiency of endocrine secretions may also alter reactions of blood vessels. Urticaria and episcleritis have been attributed to menstruation. Reynolds<sup>158</sup> reported that estrogen substances are cholinergic in that they apparently increased the acetylcholine content of the rabbit uterus. (Many persons with hypothyroidism are abnormally sensitive to cold.) Therefore, lesions attributed to endocrine imbalance may be due to angiospasm resulting from temporary failure of the hormonal mechanism concerned with maintaining homeostasis.

Histamine or histamine-like bodies are of major importance in any study of allergy for the following reasons:

- 1 The histamine theory of anaphylaxis, first formulated by physiologists, has never been disproved.

- 2 Histamine can account for all lesions attributed to allergy and focal infection.

- 3 Histamine is formed in the skin after exposure to cold. This accounts for the high incidence of allergic lesions in the winter and early spring, as well as for those which occur after a sojourn in air-cooled theaters or restaurants.

- 4 Histamine is formed in heated tissues. This explains the manifestations of allergy following treatment with heat produced artificially.

- 5 Histamine is formed in the gastrointestinal tract. Failure of the normal detoxifying mechanism provides a ready supply of histamine.

- 6 Histamine is released by antidromic nerve impulses.

- 7 Histamine is formed in traumatized tissue.

- 8 Histamine is found in leukocytes (Code,<sup>159</sup> Dale). Because of this fact, the perivascular round cell infiltration may both perpetuate the original lesion and stimulate the formation of new lesions. Such a hypothesis is particularly applicable to sympathetic ophthalmia, as I have indicated elsewhere.

- 9 Histamine intensifies positive reactions to cutaneous and intradermal tuberculin tests. Therefore, a positive reaction to the Mantoux test is not proof that an allergic ocular lesion is due to tuberculosis.

- 10 Histamine causes both arteriolar spasm and increased capillary permeability, so that plasma, white cells and, at times, red blood cells pass out into the tissues. This is the pathologic basis of allergy.

The pathologic changes of allergy are due to vascular reactions which are physiologic in nature but pathologic in degree. These vascular

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157 Spies, T. D., Bean, W. B., and Stone, R. E. The Treatment of Sub-clinical and Classic Pella, *J. A. M. A.* **111** 584 (Aug. 13) 1938.

158 Reynolds, S. M. *Science* **87** 537 (June 10) 1938.

159 Code, C. F. *J. Physiol.* **90** 349 (Aug.) 1937.

changes are the final common pathway for many etiologic agents. Probably more than one factor is operative in most cases, however, in my opinion, antigen-antibody reactions are not the cause of most allergic lesions of the eye. Many factors are of endogenous origin, and failure of homeostatic mechanisms adequately explains many cases.

A problem which requires further study is this: Why does acute uveitis occur in one person, acute choroiditis in a second and episcleritis in a third, while in still others acute retinobulbar neuritis, herpes, acute glaucoma, paralysis of an ocular muscle or acute closure of the central retinal artery or one of its branches develops, with approximately the same etiologic background for all? Except for the fact that there seems to be a definite age incidence for the occurrence of these lesions nothing further can be stated as to why these lesions develop.

I believe that allergy is a manifestation of hypersensitive vascular units and that "shock" arterioles and capillaries, rather than "shock tissues" are the basis of allergic lesions.

The treatment of ocular allergy with vasodilator substances has been productive of excellent results, both in my cases and in the cases reported by many other clinicians. Such treatment is nonspecific as regards the cause but specific as regards the pathophysiologic basis of these lesions.

#### CONCLUSIONS

The body as a whole probably has only a few simple ways of reacting to a variety of insults, whether they are chemical, bacterial, climatic or traumatic.

Ocular allergy is not a disease *sui generis*, but one which can be interpreted and investigated as a manifestation of a "morbid" physiologic state. Lesions differ in degree rather than in kind when the same tissue is involved. In different tissues the same basic pathologic process may cause superficially different lesions because of the structure of the tissue involved and its effect on the development of the lesion.

Allergy of the ocular tissues can be interpreted as a manifestation of localized vascular dysfunction.

This vascular dysfunction causes areas of localized tissue anoxia. Anoxemia is not usually, or necessarily, present.

Vasodilator therapy, which acts by relieving the tissue anoxia, seems to be of value in the treatment of the allergic lesions of the eye which have been discussed in this article. This treatment is based on the pathologic physiology of the lesions.

Further study is necessary to confirm or deny the opinions stated and the conclusions drawn from a study of the literature and from clinical research on patients.



## EXPERIMENTAL STUDIES ON THE BLOOD-AQUEOUS BARRIER

### I New Electrophotometric Method of Measuring the Concentration of Fluorescein in the Aqueous

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DURHAM, N C

THE exchange of water and other substances between the blood and the contents of the eye is not only an interesting physiologic and biochemical phenomenon but also a vital factor for the maintenance of the intraocular pressure on a certain level. In order to understand better the abnormal variations of the intraocular pressure, one should know as much as possible about the normal mechanism of the exchange of fluid between the blood and the eye, the rate of inflow of the fluid and how this rate may be changed under various conditions. Several attempts have been made to supply the blood with a tracer substance, the presence of which could be demonstrated in the aqueous after having passed through the blood-aqueous barrier. As far back as 1882 Paul Ehrlich<sup>1</sup> discovered that fluorescein injected into a rabbit's vein will appear in the aqueous after a comparatively short time. However, a controversy developed with regard to whether the mode of diffusion of fluorescein through the capillary walls really revealed the secret of how the aqueous originated and by which route and in what time it enters and leaves the eye. Whereas Ehrlich was inclined to believe that the fluorescein test would be useful for the advance of knowledge of the origin and circulation of the aqueous, Leber<sup>2</sup> was critical of its usefulness. He pointed out that by using an extremely highly diffusible substance, such as fluorescein, one would not get conclusive information on the circulation of the solvent, and therefore not of the aqueous itself. Wessely<sup>3</sup> found that there was a great difference between the concentration of fluorescein in the blood, on one side, and in the aqueous, on the other, inasmuch

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Dr W A Perlzweig, Professor of Biochemistry, gave me the use of the photo-fluorometer and other facilities of the Department of Biochemistry

1 Ehrlich, P. Ueber provocierte Fluorescenzerscheinungen am Auge, *Deutsche med Wchnschr* 8 21, 35 and 54, 1882

2 Leber, T, cited by Hertel<sup>5</sup>

3 Wessely, K. Der Flussigkeits-und Stoffwechsel des Auges mit besonderer Beruecksichtigung seiner Beziehungen zu allgemein physiologischen und biologischen Fragen, *Ergebn d Physiol* 4 626, 1905

as the aqueous always contained considerably less fluorescein than the blood. He concluded that an elective function of the ciliary epithelium, absorbing and secreting the fluorescein, was responsible for these differences. Consequently he supported the theory that the aqueous did not originate by simple diffusion through the capillary walls but was the product of a definite secretory process of the ciliary epithelium. On the other hand Yoshida<sup>4</sup> proved that when the blood serum is passed through a protein-restraining filter the filtrate contains approximately the same concentration of fluorescein as the aqueous, and Hertel<sup>5</sup> demonstrated that with an increase of blood proteins by intravenous injection of gelatin the diffusion of fluorescein into the anterior chamber was delayed. De Haan and Van Creveld<sup>6</sup> demonstrated that, also, the differences in concentration of glucose in the blood and in the aqueous have to be explained by the absorption of large amounts of glucose by the blood proteins.

After a careful evaluation of these, and a great number of other, studies, which I may be permitted to pass over in the interest of economy of space, it seems that the fluorescein test is a useful method for studying the production and circulation of the aqueous. However, when I attempted to use fluorescein for experimental studies of possible changes in the relations between blood and aqueous under the influence of certain substances, I strongly felt the lack of an accurate way of recording the concentration of fluorescein in the aqueous. Clinical observation, no matter whether daylight ultraviolet light or the beam of the slit lamp was used proved to be unsatisfactory. When several observers followed the same experiment, the opinion as to the first appearance of fluorescein in the anterior chamber and as to the intensity of fluorescein varied within considerable limits. Some authors, among them Yoshida,<sup>4</sup> used a colorimetric test by which the aqueous aspirated from the anterior chamber was compared with standard solutions, but my experience was that even so there remained a great deal of inaccuracy and arbitrary judgment. I even feel that some of the results reported by various experimenters and clinical investigators lack the power of conviction because of these shortcomings.

Recently, other substances were used as tracers instead of fluorescein. Kinsey, Grant and Cogan<sup>7</sup> used heavy water, which was given to rabbits

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4 Yoshida, Y. Ueber Wechselbeziehungen zwischen Blut und Kammerwasser, *Arch f Augenh* **100** 470, 1929.

5 Hertel, E. Ueber die Bedeutung der Ehrlichschen Fluoreszeinversuche, *Arch f Augenh* **100-101** 460, 1929.

6 de Haan, J., and van Creveld, S. Ueber die Wechselbeziehungen zwischen Blutplasma und Gewebsflüssigkeiten, insbesondere Kammerwasser und Cerebrospinalflüssigkeit, *Biochem Ztschr* **123** 190, 1921.

7 Kinsey, V. E., Grant, M., and Cogan, D. G. Water Movement and the Eye, *Arch Ophth* **27** 242 (Feb.) 1942.

by intraperitoneal injections and could be recollected quantitatively in the aqueous. An especially ingenious method, which appeals to the mind of the age of atomic fission, was devised by Kinsey, Grant, Cogan, Livingood and Curtis<sup>8</sup>. They used radioactive isotopes of sodium, chloride and phosphorus as tracer substances. However, the procedure seems to be rather complicated as these substances have to be prepared in the cyclotron by being bombarded with deuterons. Furthermore, it is not yet clear to what extent the migration of these substances really reveals the movement of water through the blood-aqueous barrier. Also, considerable differences in the rate of accumulation in the aqueous of chloride sodium and phosphorus were reported. In spite of these interesting experiments, I still believe that the fluorescein test would give the necessary information if a more accurate method of measuring the amount of fluorescein in the aqueous were available.

The first part of this paper will be devoted to the description of a new method which I developed for the measuring of fluorescein of the aqueous and its application to experimental work. The instrument used was the Model 12 Electronic-Photofluorometer<sup>9</sup>. This is an improved apparatus designed to insure strict linearity between fluorescent intensity and meter readings. It is widely used for measurements of concentration of certain vitamins. Two sets of filters are furnished, B<sub>1</sub> and PC<sub>1</sub> for measurements of thiamine and B<sub>2</sub> and PC<sub>2</sub> for measurements of riboflavin and porphyrin. Preliminary experiments revealed that for measuring fluorescein the yellow filters, B<sub>2</sub> and PC<sub>2</sub> are more suitable than the blue filters, B<sub>1</sub> and PC<sub>1</sub>. It was found that 1:8,000,000 dilution of sodium fluorescein was adequate as a standard in order to set the instrument. Although the reading appeared to be greatly reduced when the  $p_H$  of a solution was lowered below about 5, it also could be demonstrated that between  $p_H$  7 and  $p_H$  9 no appreciable difference was noted. As the  $p_H$  of the aqueous proved to be around 7.8 it is permissible to neglect the  $p_H$  when examining this fluid. (Duke-Elder<sup>10</sup> stated that the  $p_H$  of the aqueous of man is 7.5 to 7.7.)

#### EXPERIMENTS

A solution containing 0.05 Gm. of sodium fluorescein per kilogram of body weight was injected into the ear vein of an albino rabbit. To accomplish this, 0.50 cc. of a 10 per cent solution, or 0.25 cc. of a 20 per cent solution, per kilogram was used. About twenty seconds after the injection the conjunctiva and the lid

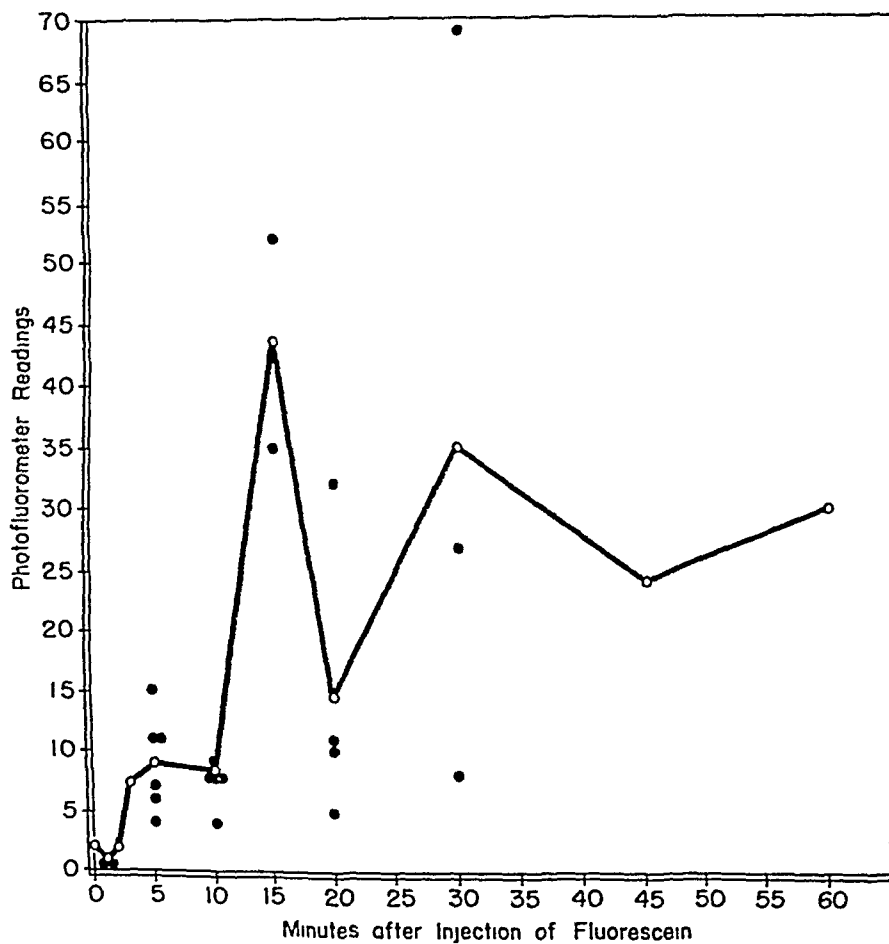
8 Kinsey, V. E., Grant, W. M., Cogan, D. G., Livingood, J. J., and Curtis, B. R. Sodium, Chloride and Phosphorus Movement and the Eye, *Arch. Ophthalmol.* 27:1126 (June) 1942.

9 Manufactured by the Colman Co., Inc., Maywood, Ill.

10 Duke-Elder, W. S. The Nature of the Intraocular Fluids, *British Journal of Ophthalmology Monograph Supplement* 3, London, George Pultman and Sons, Ltd. 1927.

margins showed a definite yellow coloration. The cornea was anesthetized with a few drops of 2 per cent cocaine, and 0.20 cc of aqueous was aspirated from the anterior chamber at various times after injection.

Each eye of an animal, of course, could be used only once during one session. It is known that the so-called second aqueous differs very much from the first one and does not show any longer the concentration of fluorescein found in the serum filtrate, called free fluorescein, but has the concentration of the serum itself, owing to its increased protein content. The same animal was not used again for at least seven days. The specimen of aqueous then was diluted with 8 cc of distilled water in order to get the minimum quantity of fluid required for the readings of the photofluorometer. After the instrument had been set at 100



Fluorescence of aqueous of rabbits after intravenous injection of fluorescein sodium. Individual readings are indicated by solid dots, average readings, by hollow dots.

with a standard solution of 1:8,000,000 of the sodium fluorescein, always freshly prepared the very day of the experiment, the diluted specimens of aqueous were examined and the readings recorded.

In the accompanying graph the results of thirty such readings are plotted.

The normal aqueous shows a slight fluorescence of its own, and up to two minutes after the injection of fluorescein no appreciable change in fluorescence was recorded. From three to ten minutes after the injection a definite increase in fluorescence appeared. Individual readings

during this period showed only a moderate discrepancy and were most uniform in about ten minutes. At the end of fifteen minutes and later the readings became rather irregular, though much increased on the average. This peculiar phenomenon is still awaiting a definite explanation. Pending further investigation, I am inclined to believe that it has something to do with the process of absorption of fluorescein by the serum proteins and its release at a certain later time. Just how this mechanism is regulated I am unable to demonstrate at present. However, for the purpose of this study, the period after ten minutes is rather irrelevant, the interval from three to ten minutes being the "critical" one, as will be seen in the second part of this paper.

#### SUMMARY

1 A new method of recording fluorescence of the aqueous after intravenous injection of sodium fluorescein, using the Colman photofluorometer, is described.

2 It is demonstrated that the diffusion of fluorescein from the blood into the aqueous of rabbits takes a fairly regular course between three and ten minutes after the injection, after which time it becomes irregularly increased.

In the second part of this study it will be demonstrated, with the method here described, how the rate of diffusion of fluorescein from the blood into the aqueous may be altered through the influence of various substances.

Duke University School of Medicine

# Clinical Notes

## A RULER FOR MEASUREMENT OF VISUAL FIELDS ON THE TANGENT SCREEN

LOREN P. GUY, M.D., NEW YORK

A TANGENT screen for charting visual fields is difficult to make and if purchased, is expensive. Plotting the measurements on a surface and painting or sewing them on requires skill in mathematics as well as manual dexterity. When completed, the marks of the measurements are usually for one distance only—1,000, 2,000 or 3,000 mm—and are set at one height. As it is often desirable to take fields with the tangent screen at more than one distance, it is an advantage to have available the measurements for 1,000, 2,000 and 3,000 mm. Tangent screens can be made so that they may be elevated or lowered to suit the height of the individual patient, but this adds to an already complicated and expensive procedure. These difficulties and shortcomings may be responsible for neglect in utilizing the valuable diagnostic and prognostic aid which tangent screens offer.

In order to obtain a ready method of charting visual fields with a tangent surface, a ruler was designed. It is simply a triangular ruler, measuring 1,500 by 20 mm. On one surface are recorded the measurements at 5 degree intervals at 1,000 mm; on another the measurements at 5 degree intervals at 2,000 mm, and on the third surface, the measurements at 3,000 mm. A schematic diagram showing the measurements between the intervals is illustrated in figure 1. The tangent screen on which the fields are to be charted is left blank except for an object for the patient's eye to fix on. This has an advantage over screens that are marked, because markings divert the attention of some patients.

To record and chart the visual fields on the tangent screen, the patient is placed at the desired distance, usually 1,000, 2,000 or 3,000 mm from a tangent surface. This surface may be a cloth screen, a blackboard, a wall or any suitable flat surface. An object, such as a white pin or a chalk mark, for the patient's eye to fix on is placed directly in front of the patient's eye. Then the fields are plotted with test objects of the same type and size as are used in a marked tangent screen, and the same procedure is followed. When the fields are plotted, the ruler is used to chart them on a suitable record. Figure 2 illustrates how this is done. Meridian lines are hardly needed for an ophthalmologist, since he is accustomed to dealing with the various meridians in refractions.

This ruler<sup>1</sup> has been used for several years and has been found to be satisfactory. It has been presented for criticism at a clinical conference of the New York Eye and Ear Infirmary and before the Section on Ophthalmology of the New York Academy of Medicine. It is felt that this ruler offers an accurate, easily constructed and inexpensive means of measuring for recording plotted tangent surface fields.

40 East Sixty-Second Street

<sup>1</sup> Clairmont & Nichols, 515 Madison Avenue, New York have made some of these rulers.

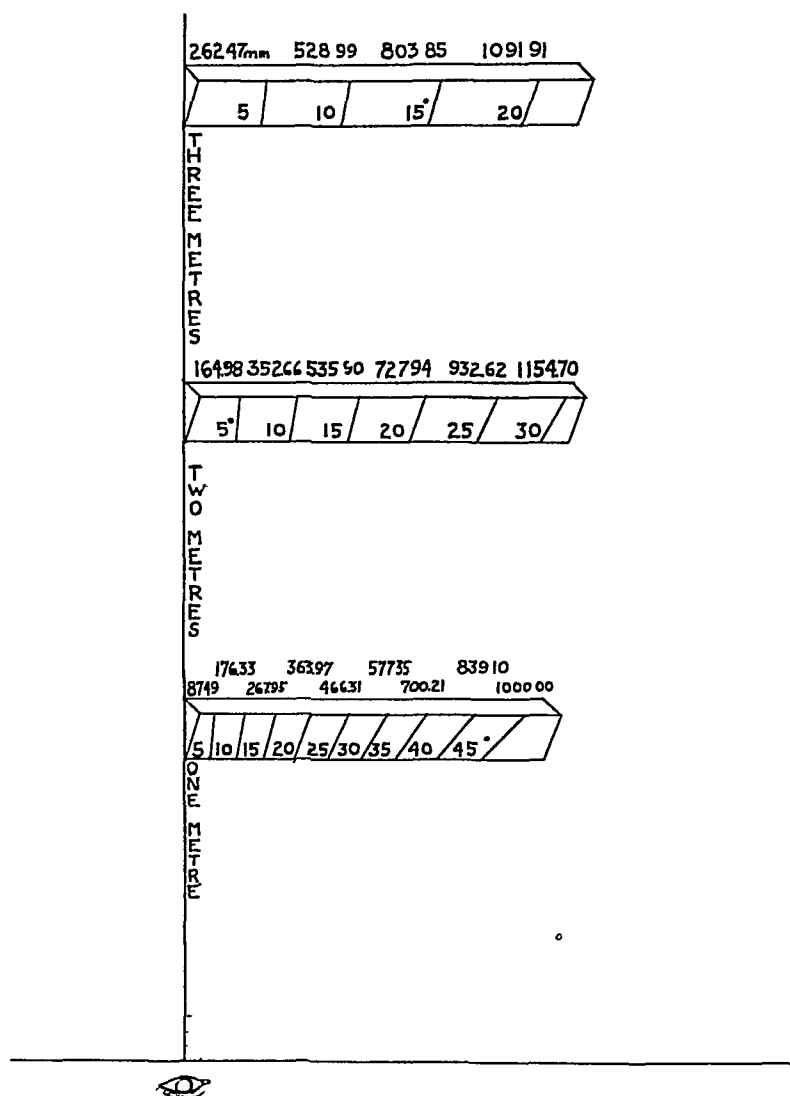


Fig 1—Diagram showing scheme of the ruler and measurements

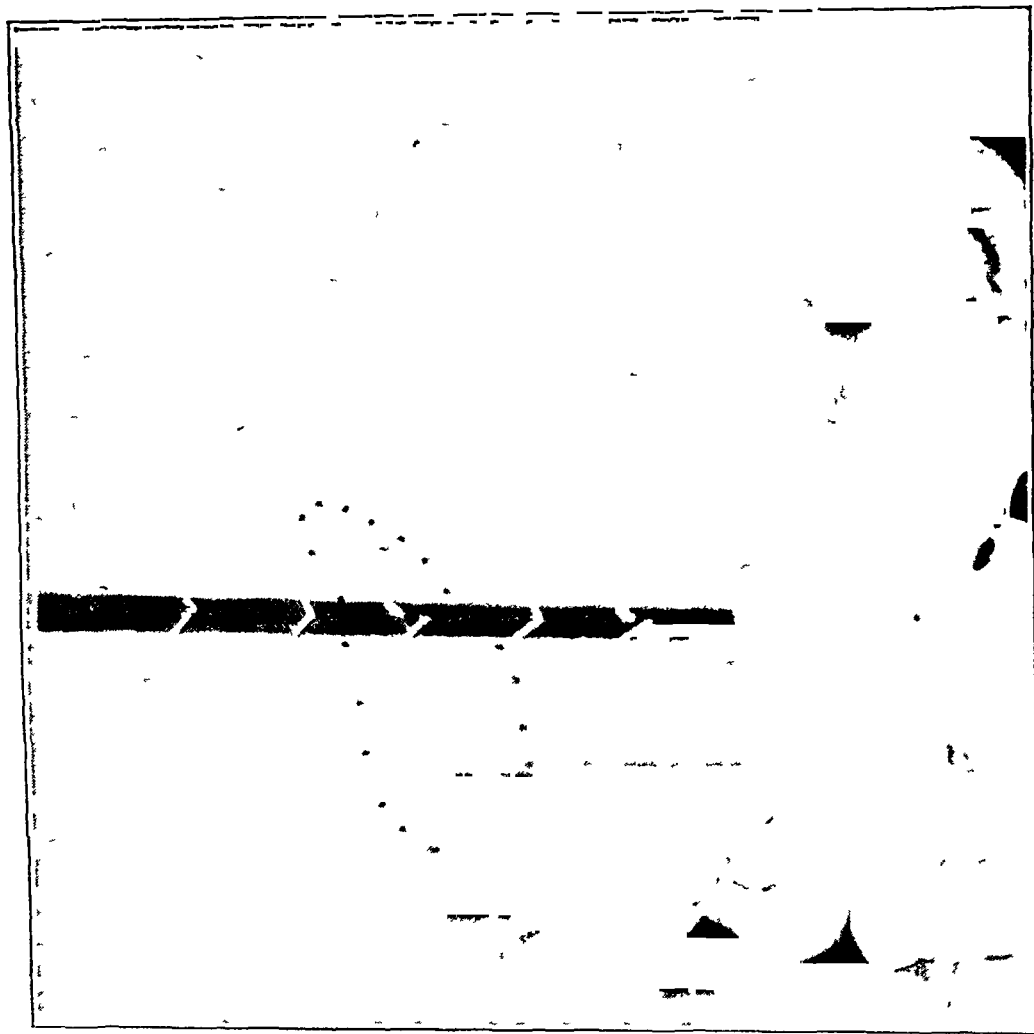


Fig 2—The ruler being used to record fields charted on the tangent field



## Correspondence

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### ALLERGIC REACTION TO SCOTCH TAPE

*To the Editor* —In the February 1941 issue of the ARCHIVES is an article in the section on "Clinical Notes" entitled "A Better Adhesive Tape for Use After Surgical Treatment of the Eye" The author rightly states that Scotch tape is a preferable substitute for adhesive tape treated with zinc oxide in applying ophthalmic dressings To further the use of this new tape in ophthalmic dressings, he emphasized the apparent freedom from allergic dermatitic reactions to Scotch tape even in patients experiencing cutaneous sensitivity to adhesive tape treated with zinc oxide

Recently, after some eight years of experience with Scotch tape and with similar tapes, I witnessed a severe allergic reaction following bandaging of both eyes The weeping, edematous and hyperemic reaction become so extensive that dressings had to be removed and the much swollen face had to be treated as a burn The eye which had been operated on reacted with an exudative reaction There was extensive regional lymphadenopathy

Investigation disclosed that the patient was also highly sensitive to adhesive tape treated with zinc oxide and to two types of Scotch tape The manufacturers presented the following analysis of pressure-sensitive tapes as containing an elastomeric component (normally some type of rubber), an adhesive component (normally a resin derivative) and an antioxidant (normally often a phenol derivative) The elastomeric component in this case was probably responsible for the allergic reaction

Prior to the war natural rubber was used exclusively In the early stages of the war various substitutes were used, including polyisobutylene During the later stages of the war synthetic rubber of the GR-S type was concentrated on More recently some natural rubber has again become available and tapes have been made of mixtures of synthetic and natural rubber It is thought that there is more danger of allergic reactions to natural rubber than to synthetic rubber

The difficulties encountered in treating the sequelae of this allergic reaction accentuate the necessity to inquire of all patients as to any previous reactions to tapes and to give the patch test to elective surgical patients at the time of their first office visit

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### REQUESTS FOR COPIES OF WARTIME ISSUES OF AMERICAN JOURNALS FOR OPHTHALMOLOGISTS ABROAD

*To the Editor* —Several months ago a notice was placed in the *American Journal of Ophthalmology* and in the ARCHIVES stating that ophthalmologists abroad would welcome the wartime issues of the American journals which were not otherwise being saved As a result sets of journals have been sent to Europe, China and the Philippines, and grateful acknowledgments have, in most instances, been received The expenses

of shipment have been borne in some cases by the senders at their request and in other cases by a fund set up for this purpose through the generosity of Mrs Elizabeth Proctor

We should appreciate hearing from any others who may wish to dispose of their wartime issues, and, as the requests come in, we shall pass them on to the prospective donors together with instructions regarding the shipments. All correspondence should be addressed to Miss Jeannette Loessl, Howe Library of Ophthalmology, 243 Charles Street, Boston 14

DAVID G. COGAN, M.D., BOSTON

243 Charles Street (14)

#### DIISOPROPYL FLUOROPHOSPHATE ("DFP") IN TREATMENT OF GLAUCOMA

*To the Editor* —The advent of diisopropyl fluorophosphate ("DFP") in ophthalmology probably marks a significant advance in the medical control of glaucoma. The disconcerting ciliary spasm and after-blur, however, will limit its field to cases of glaucoma inadequately controlled by the previously known antiglaucomatous drugs as intimated by Leopold and Comroe in their introductory article (Use of Diisopropyl Fluorophosphate in the Treatment of Glaucoma, *ARCH OPTH* 36: 1 [July] 1946).

About five months ago Dr Leopold graciously sent me a generous supply of "DFP," which my associates and I have been using in selected cases at Cook County Hospital and at the Veterans Administration Facility, Hines, Ill., as well as in private practice. The optimum results have generally been obtained with a 0.05 per cent solution administered morning and evening. Stronger solutions cause more discomfort, and in cases in which the 0.05 per cent concentration has failed to lower the tension sufficiently, stronger solutions have not been more effective. It is also possible that a too intense ciliary spasm, or the pain on these occasions, may have an adverse effect. I recall an elderly patient with acute glaucoma who had achieved comfort, with a tension of 35 mm., with a 0.25 per cent solution of physostigmine salicylate, after the substitution of 2 per cent physostigmine nitrate, at the suggestion of a consultant, acute pain followed, and the tension rose to 65 mm. Though the miosis from "DFP" lasts several days the intraocular tension usually reaches its lowest in twelve to fifteen hours, so that in the average case instillations morning and night constitute the logical treatment. However, some patients with moderately elevated tensions required but one instillation daily. Other patients who at first reacted brilliantly later failed to respond even with more frequent use and with stronger solutions.

In most cases of secondary glaucoma, including uveitis, rubeosis iridis and occlusion of the central retinal vein, use of "DFP" proved futile. But in 2 cases of morgagnian cataract in which pilocarpine had lowered the tension from 70 to 30 mm., "DFP," instilled once daily, reduced the tension to 14 mm. The cataract operation was then done, with uneventful recovery. Of 3 cases of glaucoma following cataract extraction in which pilocarpine and physostigmine had been ineffective, "DFP" successfully lowered the tension in 2. In the third case a tension of 62 mm. had also persisted after a previous cyclodialysis.

The very high tensions may respond only slightly to use of "DFP" A woman with chronic simple glaucoma and a tension of 101 mm in each eye was treated with physostigmine and pilocarpine without any change in her condition With use of "DFP" (0.05 per cent four times a day for five days) the tension became only 86 mm in the right eye and 101 mm in the left eye

In normal eyes atropine cycloplegia, whether produced by instillation or by internal medication, may be more than counteracted by 0.1 per cent "DFP" and in 2 instances homatropine had to be instilled to reduce the persisting ciliary spasm and photophobia But for relief of glaucoma precipitated by atropine the drug has only slight value A diabetic patient with amblyopia of the left eye from hemorrhages in the vitreous was treated with atropine for a corneal ulcer in this eye Though the ulcer healed the eye became excruciatingly painful The tension then taken was 45 mm in the right eye and 118 mm in the left eye Three days later, after use of "DFP," the tension was 17 mm in the right eye and 86 mm in the left eye and the pupillary diameters were 1.5 and 4 mm, respectively The pain in the left eye was then relieved by a retrobulbar injection of 0.5 cc of 60 per cent alcohol and use of "DFP" was continued, but during ten days of observation the pupil contracted no further and the tension did not decrease below 75 mm

We have found that the prompt and persisting miosis produced by one application of 0.05 per cent "DFP" at the conclusion of operation makes this drug the miotic of choice in the intracapsular extraction of cataract through a round pupil and in cyclodialysis

JAMES E. LEBENSOHN, M.D., CHICAGO

4010 Madison Street

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## News and Notes

EDITED BY DR. W. L. BENEDICT

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### SOCIETY NEWS

**Philippine Ophthalmological and Otolaryngological Society**—The Philippine Ophthalmological and Otolaryngological Society has been formed, and the inaugural meeting was held on Jan. 26, 1946, at the Gauzon Memorial Hall, Philippine General Hospital, Manila.

The following officers were elected: president, Antonio S. Fernando, M.D.; vice-president, Edmundo Reyes, M.D.; secretary-treasurer, Jose N. Cruz, M.D.; directors, Germiniano de Ocampo, M.D., Tomas Hano, M.D., Jesus Eusebio, M.D., and Gregorio Farrales, M.D.

Meetings will be held in January, March, May, July, September and November.

### GENERAL NEWS

**Twentieth Annual Spring Graduate Course in Ophthalmology and Otolaryngology**—The annual spring graduate course in ophthalmology and otolaryngology will be held at the Gill Memorial Eye, Ear and Throat Hospital, Roanoke, Va., April 7 to 12, 1947.

# Abstracts from Current Literature

EDITED BY DR WILLIAM ZENTMAYER

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## Cornea and Sclera

UNUSUAL TYPE OF CORNEAL OPACITIES J W HENDERSON and D R GILLESPIE, *Am J Ophth* 28:1236 (Nov) 1945

Henderson and Gillespie report 8 cases of temporarily blurred vision due to fine brownish opacities in the cornea. Microscopic examination of the eye of a patient who died of hepatitis showed that these opacities were scattered along the posterior endothelial layer of the cornea. No evidence of systemic disease or avitaminosis was found.

W S REESE

A CASE OF MUSTARD GAS KERATITIS TREATED WITH CURETTAGE OF THE CORNEA FOR THE REMOVAL OF A BAND-SHAPED CRYSTALLINE DEPOSIT H NEAME, *Brit J Ophth* 29:102 (Feb) 1945

Neame reports this case because it has become customary to regard cases of severe mustard gas (dichloroethyl sulfide) keratitis unsuitable for operation because of the liability to recurring ulceration.

A man aged 56 was fitted with contact lenses on account of progressive deterioration of vision. Visual acuity in the left eye was 3/60, owing to a transverse band on the cornea extending across and below the pupillary area, composed of a superficial deposit of crystalline appearance and completely obstructing the vision. After curettage of the opacity vision gradually increased until, two years later, it was 6/36 with a contact glass.

W ZENTMAYER

## General

A REVIEW OF EYE DISEASE IN CENTRAL CHINA G H PEARSON, *Brit J Ophth* 29:260 (May) 1945

The basis of this review is experience during a residence of twenty-four years in Shaoyang, Hunan, Free China, in which Pearson's main interest has been ophthalmology. The great bulk of the cases has always been those of conjunctival infections and their sequelae. Between 1929 and 1942, 1,341 inpatients were treated for trachoma, 1,027 operations were performed for entropion and 51 operations for cataract. The treatment of diseases of the fundus and the prescription of glasses have assumed a minor role, owing to social conditions. The call for properly adjusted glasses is increasing, and it is now possible to get glasses ground locally by Chinese firms.

The cases of trachoma are separated into cases of the early form, with only rudimentary formation of follicles and with, as yet, no macroscopic pannus formation, cases of fully developed trachoma, cases of the cicatricial stage, in which the follicles have mostly disappeared and scar

tissue has taken their place, and cases of the "hard type of trachoma," in which the fibrous tissue takes on a hard, nodular condition and when fully developed looks like a tessellated pavement (probably the "spring catarrh" described in textbooks, but in Hunan it definitely belongs to the trachoma family), and cases of a late degenerative condition, the formation of a plasmoma. In China a pterygium often is a late complication of the multiple irritations of trachoma, though it may in theory occur without trachoma.

After trying out most of the operations for entropion, the author now uses almost uniformly the Hotz operation.

Trachoma with its sequelae is one of the greatest causes of ultimate blindness in Free China.

W ZENTMAYER

#### USE OF MIXTURE OF ENCODAL, SCOPOLAMINE AND EPHETONIN IN OPHTHALMOLOGY POYALES, Arch Soc oftal hispano-am 4: 365 (May-June) 1944

Poyales uses this combination of drugs to induce twilight sleep for certain operative procedures in ophthalmology. Encodal is a codeine derivative (dehydrooxycodeme), a substitute for morphine in the morphine-scopolamine mixture. It is more analgesic and less toxic, although more likely than morphine to produce habit formation. To this mixture ephedrine or Ephetonin (an isomer of ephedrine) is added as a stimulant to the respiratory and cardiac centers, to counteract the depressing action of scopolamine.

The combination is used in cases of acute glaucoma while the proper time for surgical intervention is awaited and also as a preliminary to probable painful operations, such as dacryocystorhinostomy, exenterations for panophthalmitis and retinal detachment.

H F CARRASQUILLO

### General Diseases

#### OCULAR COMPLICATIONS OF CERTAIN TROPICAL DISEASES M J REEH, Am J Ophth 28 958 (Sept) 1945

An abstract of the author's summary follows.

After World War II physicians may encounter tropical diseases which are rare or unknown in the United States. These will be found in men who have served in the armed forces overseas or among persons who will travel extensively because of the vast postwar development of highways and air lines. Any one ophthalmologist will see an extremely limited number of cases, however. Fortunately, ocular complications are found to occur with only a few of the many tropical diseases.

Malaria is believed to be one of the causes of dendritic keratitis. At the present time clinical observations are not conclusive. The true etiologic basis is still vague. Other ocular complications of malaria are rare. The more serious complications result from the administration of quinine to sensitive persons.

African trypanosomiasis will probably always be extremely rare in the United States, however, the final outcome in untreated patients is so disastrous that it is well for all physicians to be on the alert.

Filarial diseases are extremely common in various parts of the world. Despite the widespread existence of *Wuchereria bancrofti*, cases of entrance of this worm into the globe are rare. The adult *Loa loa* lives in the body for many years. It wanders freely about in connective tissue, frequently appearing beneath the skin of the lids or the conjunctiva—hence the old name *Filaria oculi*. It does not tend to enter the globe itself, however. *Onchocerca volvulus*, on the other hand, is destructive to the eye. The microfilarias enter the layers and chambers of the eye readily, producing inflammation which not infrequently results in blindness. Onchocerciasis may prove to be more troublesome in the future because of increased travel into areas of Mexico and Guatemala where the disease is endemic.

Reeh reaches the following conclusions. Certain tropical diseases produce ocular complications. Such complications may be improperly evaluated and inadequately treated because the causative disease is not recognized.

W ZENTMAYER

ROLE OF FOCAL INFECTION IN OPHTHALMIC DISEASE J PEREIRA  
GOMES, *Arq brasil de oftal* 7:201 (Dec) 1944

A historical summary of the subject is presented. A personal observation on a patient aged 22, who was blind in the right eye, is given. After removal of the upper row of teeth, all of which were infected, vision returned to 9/10. The author states that, in his opinion, the upper teeth when infected can cause more damage than the lower. When there is suspicion of focal infection, other probable foci should be sought for, and the patient should be requested to submit to laboratory examinations. In the case of dental foci a close collaboration between dentist and ophthalmologist is desirable. The duty of an ophthalmologist, however, lies in removing every possible cause of the ocular lesion, for, although certain foci may not be entirely responsible for the ocular diseases, their removal will benefit the patient's general health.

M E ALVARO

Hygiene, Sociology, Education and History

READING DISABILITY A PEDIATRIC PROBLEM T H WOLF, *Journal-Lancet* 65:184 (May) 1945

Wolf shows that disability in reading may play a part in the physical complaints and emotional tensions found in school children, particularly in those 9 to 10 years of age or older. From the fourth, fifth and sixth grades on, the ability to read assumes an increasingly important part in nearly every school subject. A youngster unable to compete with his classmates because he cannot read finds himself at a disadvantage, and repeated failure results in unhappiness, for which he may try to compensate in various ways. He may present a behavior problem, becoming sullen and negativistic toward his teacher and classmates. He may become the bully or withdraw from contacts with the group. On the other hand, he may have bizarre physical complaints, varying from mild headaches to severe digestive disturbances, fainting spells or convulsive seizures. He may manifest both emotional and physical symptoms. A case recently encountered in the pediatric outpatient

department of the University of Minnesota Hospitals illustrates the point. A frequent error of parents and teachers is to think of the child as dull and stupid. Measured intelligence and rapid progress in school after remedial treatment have proved otherwise. Uncorrected conditions of the eye or ear may be responsible for the reading difficulties. The physician should look for muscular imbalance, which may cause a lack of fusion of visual images. Some children need additional corrective training of ocular muscles. Islands of deafness may be recognized. Other factors that play a part in reading disability are inadequate instruction, emotional problems and cerebral factors. The theory that the causative factor was left handedness, a mixed eye-hand dominance in the cerebral hemispheres, has been open to serious question and criticism. Most, if not all of the difficulties can be relieved with proper guidance.

J A M A (W ZENTMAYER)

### Injuries

CHRONIC POSTTRAUMATIC SYNDROMES LEADING TO ENUCLEATION  
B A KLIEN, *Am J Ophth* 28 1193 (Nov) 1945

Among the inflammatory and other post-traumatic chronic conditions that led to enucleation of the 77 eyes reported on in this series, nonspecific infiltrating iridocyclitis, far from being the most frequent condition encountered, occurred in only 17 eyes, or 22 per cent. More frequent was chronic septic endophthalmitis, present in 20 eyes, or 26 per cent. Four other conditions accounted for more than one third of all the enucleations, namely, epithelial implants (12 per cent) and chronic hemophthalmos, extensive contusion necrosis and late toxic iritis after long-standing retinal detachment (8 per cent each). Endogenous iridocyclitis occurred in 5 per cent of the eyes, and some rarer conditions were present in a total of 3 per cent. Sympathetic ophthalmia itself occurred in only 6 eyes, or 8 per cent (less than 3 per cent of the 219 penetrating injuries).

There was no evidence in any of the eyes in this series to suggest that they could have been saved.

W S REESE

TREATMENT OF PERFORATING WOUNDS AND BURNS OF THE EYE WITH  
LYSOZYME E CHECHIK-KININA, *Vestnik oftal* 24 42 1945

The titer of the lysozyme of the tears was determined in 25 eyes with penetrating injuries, as well as in normal eyes. The lysozyme content was lowered considerably in 23 eyes, as compared with the titer of the tears of normal eyes. The infection was in inverse proportion to the lysozyme content, i e., the higher the lysozyme content, the lower was the number of ocular infections.

Lysozyme was used in the form of instillations, ionization and injections into the anterior chamber in 54 patients with perforating wounds of the eye. This prophylactic treatment gave good results, as only 12.7 per cent of the eyes were lost.

Lysozyme was also used in treatment of burns of 31 eyes, in only 3 eyes with very severe burns (necrosis of the tissues) was the lysozyme therapy not effective.

Experimental tests on 10 rabbits verified the beneficial effect of lysozyme in treatment of burns of the eye

The following conclusions are drawn The titer of lysozyme as a rule is lowered in cases of perforating ocular injuries

The number of infections associated with perforating injuries of the eye is in direct ratio to the lowered titer of lysozyme of the tears

The titer of the lysozyme of the tears has a definite prognostic value

The treatment of perforating injuries of the eye with lysozyme gave favorable results

The treatment of mild and severe burns of the eye with lysozyme was quite effective Only in 3 eyes with extremely severe burns did the treatment give negative results

Experimental work on rabbits confirmed the value of lysozyme in burns of the eyes

O SITCHEVSKA

### Lacrimal Apparatus

RHINOSTOMY AND ITS INDICATIONS E M IVANOVA, Vestnik oftal 24: 12, 1945

This article is a tribute to the late professor Averbach who was the pioneer in Soviet Russia in the use of dacryocystorhinostomy From 1926 to date there were performed 6,000 rhinostomies Averbach stated that a large hole in the nasal bone (1.5 by 1.5 cm) is the most important factor in obtaining the best end results The sutures in the mucous membrane are of secondary importance

Averbach expressed his belief that there are hardly any contraindications to this operation It is especially indicated in cases of recurrent phlegmon of the sac, as the dacryocystitis and the phlegmon are done away with It is not difficult to perform the operation on aged people Because of the fragility of the bone, it is easy to make the opening in the bone

Successful results were obtained in 97 per cent of cases The unsuccessful results in 3 per cent were due either to too small an opening or to an incorrect position at the opening in the bone

O SITCHEVSKA

### Methods of Examination

A SIMPLE DEVICE FOR TESTING DIPLOPIA I C MICHAELSON, Brit J Ophth 29: 376 (July) 1945

The device consists of a cap with an arrow-shaped perforation, the opposite inner wall is painted white to reflect the internal light The cap fits over the lamp end of the ophthalmoscope A 10 inch (25.4 cm) pendant string, weighted at its end, is marked into inches with small pieces of metal The distance between the false and the true image can be found by asking the patient to touch the arrow and then point to the false image The distance between the arrow and the patient's finger is measured on the string The degree of tilting of the false image can be found by tilting the handle of the lamp until the false image is erect and then noting by touch the angle between the handle and the dependent string

The article is illustrated

W ZENTMAYER



### Neurology

#### HYSTERIA IN OPHTHALMOLOGY EXPERIENCES WITH NEW ZEALAND TROOPS IN THE MIDDLE EAST H COVERDALE, Brit J Ophth 29 120 (March) 1945

Among 58,927 troops which constituted the New Zealand expeditionary force to the Middle East up to the end of November 1943, 95 had a condition diagnosed as hysteria, in 50 of whom it was considered severe and in 45 mild. The average age was 30 years. Of the 95 men, 62 had not been in action with the division, while the remaining 33 had been with the division in the field, though not necessarily in action in the face of the enemy, very few had been sent back to base because the disability had occurred during combat. The majority had paraded sick, and the diagnosis had been made soon after their arrival in Egypt. The most interesting fact to emerge from the clinical examination of these men was that a high proportion had some preexisting ocular defect, dating in most cases from childhood. It may be that such ocular disabilities tend to make men susceptible to hysteria or, on the other hand, that in persons who are prone to hysteria from heredity, environment or other causes, the disability tends to appear in that organ which the man, consciously or unconsciously, believes to be weak.

W ZENTMAYER

#### AMBLYOPIA WITH HYDROCEPHALUS K N PRADHAN, Indian J Ophth 6 11 (April) 1945

In a case of acute hydrocephalus, possibly of malarial or filarial origin, in an infant 3 weeks old, there was in the right eye a gray-white atrophy of the optic nerve, and in the left eye congestion of the disk. Two years later there was marked atrophy of the optic nerve in both eyes, though the child could recognize people at 20 feet (6 meters). As modern treatment will save an increasing number of patients with serous meningitis, the problem of preserving the vision of such patients confronts one.

W ZENTMAYER

### The Pupil

#### SEGMENTAL MOVEMENT OF THE PUPIL IAN S MCGREGOR, Brit M J 1 629 (May 5) 1945

Segmental movement, or twitch, at the pupillary margin was first described by Sattler, in 1911. It is seen in the pupil which has no normal reaction to light or in which the response to light is much diminished. Sometimes only a single twitch is apparent, in other cases a similar twitch may appear at another place in the pupillary margin. The worm contraction, or undulate contraction, of the pupillary border is much less common. These changes are readily observed with the use of a low power magnifying loupe or microscope. Patients with partial loss of field after head injury and patients with glaucoma showed no segmental movement. A number of patients were examined in order to determine whether the sign had any localizing value. These included persons with syphilitic atrophy of the optic nerve, post-

traumatic atrophy of the optic nerve, Leber's disease, blindness due to quinine (1 patient), retrobulbar neuritis, and unilateral Adie's pupil (2 patients)

This disturbance is associated with sufficiently severe disorders of the afferent or efferent nerve paths to the sphincter of the pupil. It is not seen in the contracted pupil. It may be due to diminished conduction in the nerve paths to the sphincter pupillae, or there may be a pathologic variation or inequality of flux within the nerve plexus.

The author concludes that "the sign, so far as this short investigation will allow us to conclude, will not appear to have any localizing value, it is a fibrillation of the pupil resulting from impaired integrity of the nervous arc of the sphincter pupillae occurring at any part of the arc."

ARNOLD KNAPP

### Refraction and Accommodation

RELATIONSHIP BETWEEN VISUAL ACUITY AND REFRACTIVE ERROR IN MYOPIA J S CRAWFORD, C SHAGASS and T J PASHBY, *Am J Ophth* 28:1220 (Nov) 1945

An abstract of the authors' summary and conclusions follow

Data showing the quantitative relation between refractive error and visual acuity were presented for 325 eyes with simple myopia, 160 eyes with simple myopic astigmatism and 714 eyes with compound myopic astigmatism.

The results showed that visual acuity and refractive error are closely related, although factors other than refractive error influence measurements of visual acuity.

The data presented here permit for myopia the construction, in terms of refractive error, of visual standards which may be used to supplement the usual statement of such standards in terms of the Snellen test.

W S REESE

### Retina and Optic Nerve

THROMBOSIS OF CENTRAL RETINAL VEIN H J STERN, *Brit J Ophth* 28:643 (Dec) 1944

The case is reported to emphasize a warning regarding undue optimism in therapeutic attempts, especially in cases of younger persons, and to show that the complete spontaneous recovery from a serious condition is certainly possible and so-called cures should always be regarded with skepticism.

A physician aged 24 awoke with poor vision in the left eye. Ophthalmoscopic examination showed pronounced venous congestion of the retina with some hemorrhages. Vision was reduced to 2/60. The visual field was contracted concentrically. On his rising from the table after a roentgenographic examination, vision was found to be 6/12, the visual field nearly normal and the ophthalmic picture unchanged.

Several days later vision was again 2/60, and the fundus showed the fully developed picture of thrombosis of the central retinal vein. Vision slowly improved without treatment, so that after eight or ten weeks it was restored to normal and the visual field was only slightly constricted.

Three years have elapsed since this episode, the patient has remained in the best of health, and his eyesight has not changed. Photographs of the fundus showing the initial condition, the appearance when the thrombosis was at its height and the appearance after eight weeks are included

W ZENTMAYER

#### ILLUMINATED ELECTRODE FOR RETINAL DETACHMENT OPERATION T COLLYER SUMMERS, Brit M J 1 48 (Jan 13) 1945

The author believes that an incorrectly applied electric current explains macular degeneration and other field defects which occur after successful operations for detachment. He recommends that the hole be found by transillumination. A transilluminator designed by Gray Clegg, of Manchester, England, was modified so that the naked light was covered with ground glass. This reveals a hole in the macula clearly. Then it was decided to add an electrode around the light, as is well shown by the illustration which accompanies the article.

After the incision is made through the conjunctiva and Tenon's capsule on the outer side of the globe, the external rectus muscle is divided. The electrode transilluminator is then introduced, while the operator, with a nonilluminated ophthalmoscope, examines the fundus, when the light is opposite the hole, the current is turned on at 120 milliamperes for five seconds. Two applications are made, so that the hole is properly covered. Fluid is then let out with a diathermy needle of 2 mm thickness and suction applied. It is important, before introducing the transilluminator, that the sclera be dry and free from blood.

ARNOLD KNAPP

### Therapeutics

#### CHOLINERGIC DRUGS AND KERATOPLASTY F VIDAL and J MALBRÁN Arch de ofal de Buenos Aires 19 409 (Oct) 1944

From their experience with keratoplasty, the authors conclude that the postoperative glaucomatous state which at times occurs in eyes on which keratoplasty has been carried out may take place without the presence of anterior synechia, which is considered the causative factor by most authorities. The authors believe that a disturbance in the nutrition of the cornea, thereby lessening its permeability, is at times the origin of the hypertension. This nutritional disturbance of the cornea is favorably influenced by the use of cholinergic drugs. The authors report 4 cases in which this treatment was used, in 3 of which good results were obtained.

H F CARRASQUILLO

# Society Transactions

EDITED BY DR W L BENEDICT

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COLLEGE OF PHYSICIANS OF PHILADELPHIA, SECTION ON OPHTHALMOLOGY

Burton Chance, M D , *Chairman*

George F J Kelly, M D , *Clerk*

*April 18, 1946*

**Stevens-Johnson Disease: Report of a Case** DR BRUCE A GROVE  
and DR EDMUND MEISENHOLDER (by invitation)

Stevens-Johnson disease is generally considered a manifestation of erythema multiforme exudativum, first described as a clinical entity by von Hebra in 1866. The lesions occur in the conjunctiva as well as on the mucous membranes of the mouth, nose, pharynx, larynx, trachea, bronchus and genitalia. Conjunctivitis may be the first symptom of the general disease, and according to Duke-Elder it may take three forms, namely, a relatively mild catarrhal, a purulent and a severe pseudomembranous form.

The first recorded case of ocular involvement was described by Fuchs in 1876 as "hepides iridis conjunctivae."

*Staphylococcus aureus* is more commonly found on culture than any other organism.

The disease is of sudden onset with high fever and pronounced constitutional symptoms, which gradually subside, and the patient usually recovers in eighteen to twenty-one days. Although prostration is severe, the mortality rate is low, only 4 deaths having been reported.

A review of the literature illustrates the confusion existing among authors as to the proper cataloging of the disease.

The case reported is that of a white man, aged 30, who first complained of light hurting his eyes. Examination revealed mild injection of the palpebral and bulbar conjunctiva. Within twenty-four hours he was violently ill, and his temperature rose to 103.2 F. There was a cutaneous rash, consisting of macules, papules and intracutaneous vesicles. Involvement of all the mucous membranes and mucocutaneous junctions and severe pseudomembranous conjunctivitis were noted.

The patient was discharged on the twenty-first day after onset with no loss of visual acuity, but with slight symblepharon, prominent scarring of the palpebral conjunctiva and occlusion of all the puncta.

Drug and serum reactions were ruled out as causative agents. Acute vitamin deficiency was suggested as an etiologic factor.

The authors concluded that Stevens-Johnson disease is a severe form of erythema multiforme exudativum with involvement of the conjunctiva, whether it be catarrhal, purulent or pseudomembranous.

Several slides were shown.

## DISCUSSION

DR JOHN F WILSON As the authors have stated Stevens-Johnson disease is considered by many authorities to be erythema multiforme, and the slides well demonstrate the extensiveness of involvement which may occur in this disease. Not only were bullae present, but there were various other lesions on the skin, namely, macules, papules and pustules. Erythema multiforme produces multifocal lesions, which may involve any of the dermal areas or the mucous membranes. The disease is thought to be due to a virus, although the virus has never been demonstrated. It is possible that in the authors' case a dietary deficiency lowered the patient's resistance so that such a virus gained a foothold.

It is important to differentiate the changes in the eyes in this case from those occurring with pemphigus vulgaris. Three outstanding characteristics not directly related to the ocular structures, of this case will differentiate the disease from pemphigus vulgaris. First, as Dr Grove mentioned, pemphigus usually occurs in older patients. This patient is now 30. He was about 28 at the time of the attack. Second, the onset of the disease, unlike that of pemphigus, was sudden and severe. Within twenty-four hours it had almost reached its peak, and from that time on the patient's condition gradually improved. Third, the entire course of the disease lasted nineteen days. Pemphigus, however, is characterized by a longer term, with exacerbations and remissions and ultimately a fatal outcome.

There is one type of pemphigus which could easily be confused with this condition, that is pemphigus of the mucous membranes, or localized pemphigus. This type is characterized by outbreaks of bullae in various areas, involving only small areas at a time. There are then relapses, with similar small areas becoming involved, but ultimately the reaction becomes generalized. The whole of the skin and mucous membranes is affected, and the disease terminates fatally. The course is chronic.

As Dr Grove mentioned Duke-Elder, in his conclusions, divides the ocular involvement of erythema multiforme into three types: the catarrhal, the purulent and the pseudomembranous. He believes, and most of us would agree with him, that these are differences of degree rather than of type. In other words, the pseudomembranous type shows the most severe changes involving the ocular structures. That point is aptly demonstrated by the penile lesion in this case. It bears a close relation to the ocular lesion and shows a similar bandlike scar, holding down the prepuce to the glans.

DR W ZENTMAYER I shall not discuss the paper itself, but I want to comment on the title. This is not a criticism of the authors, for they have a precedent for their use of the name. It seems to me, however, that when a general disease has common ophthalmic complications to make an entity out of cases in which those complications are a little more severe is of questionable validity. One might just as well speak of the Wheeler syndrome, for in Wheeler's case the disease was much more severe than usual, with development of panophthalmitis and loss of the eye. It seems to me that it is hard to justify the establishment of an entity for this group of cases of erythema multiforme.

exudativum Furthermore, there is an objection to the use of an author's name to designate a syndrome It gives no indication of the nature of the disease, and when one is searching the literature for a certain condition one may overlook cases that are published under a syndrome bearing an author's name

DR BURTON CHANCE I agree with Dr Zentmayer, for it would be difficult to know to what condition the names of these two men refer The title would have been understood if it had denoted a special type of erythema multiforme I have seen this disease in a general way, but in no case was the eye involved as it was in the one which has been so interestingly presented

**Acquired Ophthalmic Allergy.** MAJOR WILLIAM F BONNER, Medical Corps, Army of the United States (by invitation)

- 1 Acquired allergy may be single or multiple
- 2 The most common offender is atropine, which may cause dermatitis or intraocular hemorrhage
- 3 Quinine amblyopia may be acquired, and in the case which was reported the condition was helped by administration of 50,000 units of vitamin A three times daily
- 4 Hemorrhagic allergy was improved by use of Padutin (a pancreatic preparation)

**Keratitis Associated with Lymphogranuloma Venereum** DR HAROLD G SCHEIE and (by invitation) DR ALAN S CRANDALL

Four cases were discussed in which identical corneal lesions of a distinctive type were associated with lymphogranuloma venereum Evidence supporting the designation of the virus of lymphogranuloma venereum as the etiologic agent was considerable

- 1 The corneal lesion was so characteristic as to suggest the diagnosis of lymphogranuloma venereum in all the cases
- 2 Diagnosis of the systemic disease was further established by additional clinical or laboratory evidence or both
  - (a) In all cases the Frei test gave a positive reaction
  - (b) In 2 cases scars of healed buboes and in 1 case active inguinal involvement were present
  - (c) In the fourth case, there was no clinical evidence of lymphogranuloma venereum other than a strongly positive complement fixation reaction, and biopsy of the corneal lesion showed histologic changes compatible with the disease
- (3) The corneal lesion was always associated with a positive reaction to the Frei test and never with any disease other than lymphogranuloma venereum
- (4) The lesions were identical with those occurring in a case of lymphogranuloma venereum reported by Meyer and Reber in 1940

#### DISCUSSION

DR WERNER HENLE My colleagues and I are glad to have had the opportunity to study in the laboratory 1 of the cases just presented The

results we have obtained thus far serve well to demonstrate the possibilities, as well as the limitations, of laboratory studies in the diagnosis of virus infections

There are three general approaches to the laboratory diagnosis of a virus disease (a) isolation and identification of the causative agent, (b) determination of the serologic response of the patient and (c) demonstration of characteristic pathologic lesions. We have used all three avenues in this case, and in discussing it I shall begin with the third approach, the demonstration of characteristic lesions. Part of the material obtained for biopsy from the cornea was sectioned and stained with Giemsa's method (two slides). On examination many epithelial cells, and in some regions of the section practically all of them, contained cytoplasmic inclusions. These consisted of aggregations of small round bodies staining dark purple. In many places individual bodies or small groups of these particles were observed. They had a diameter of from 200 to 300 microns and represented probably the elementary bodies of the virus involved in this case. Such inclusions occurring with lymphogranuloma venereum were first fully described by Miyagawa as "granulocorpuscles."

The patient's serologic reactions were likewise in accord with what one would expect to find. The complement fixation test with Lygranum antigen (a brand of chick embryo antigen) gave a high serum antibody titer (1:256). The antigen used is the same material which is employed in the Frei test, which also gave a positive reaction, as the authors have pointed out.

Our studies on the isolation of the causative agent have not yet been completed. The number of elementary bodies visible in the section would imply that the virus should be isolated with ease. On the other hand, the high antibody level of the patient's serum may cause considerable difficulty. In order to release the virus from the cells, the tissue has to be emulsified by grinding in a mortar with an abrasive, and it is impossible to avoid the contact of antibody with the virus, thus, some virus may be neutralized before the injection of the emulsion into experimental animals.

The first attempt at isolation of the virus was made by intracerebral injection into white mice. No lesions developed and on the twelfth day the animals were killed and their emulsified brains passed to new mice. Again no lesions developed, and this line of investigation was discontinued.

A second attempt was made with the chick embryo. In this study, the remaining biopsy material, which had been kept at  $-10^{\circ}\text{C}$ , was injected into the yolk sac of 8 day old chick embryos. They survived eight days of further incubation, when the yolk sacs were harvested. A 20 per cent suspension was passed to new eggs, and also to white mice, by the intracerebral route. The mice showed some signs of cerebral lesions on the fourth and fifth days. They lost weight, and on suspension by the tail they exhibited tremor and had difficulty in regaining equilibrium on release. Passage of the emulsified brains of these mice to other mice produced severer lesions and death. At this point of the investigation we now stand. There is clearly a chance that the agent has been isolated from the biopsy material. If so, it has to be identified by neutralization of the agent with known specific

immune serums as well as with the patient's serum. The possibility of having activated a latent virus in the mice must be excluded.

What do the various data imply? The virus of lymphogranuloma venereum belongs to a group of agents which have been classified together on the basis of various properties they have in common. In this group of agents are found, besides the virus of lymphogranuloma venereum, the agents of psittacosis, ornithosis, meningopneumonitis, trachoma, inclusion blennorrhea, mouse pneumonitis and other virus diseases. They all form similar cytoplasmic inclusions and exhibit serologic cross reactions. Neutralization of the toxic activity of these agents, described by Rake and Jones, constitutes the most specific test and serves best to differentiate the various viruses of this group.

From the data presented, there is little doubt that the agent involved in the case presented belongs to this group of viruses, but we cannot yet say with definite assurance that it is a strain of the virus of lymphogranuloma venereum. Although all results seem to be in accord with this diagnosis a differentiation of the various inclusions cannot be made with sufficient accuracy. The high complement fixation titer with Lygranum antigen appears significant but may not be out of the range of cross reactions observed with some of the other viruses of this group. Fairly strong cross reactions with Lygranum antigen have been reported, for instance with serum from patients with psittacosis and pneumonitis. The Frei test, too, has been found to give a weakly positive reaction in some cases of psittacosis, meningopneumonitis and atypical pneumonia. The final diagnosis hinges on the isolation and characterization of the causative agent. This has not been accomplished as yet, but, as I pointed out, there is a good chance that we may be successful.

DR I. S. TASSMAN: I should like to ask the authors whether they observed the characteristic conjunctival lesion also in any of these cases of lymphogranuloma venereum. I believe that the typical lesion of this disease occurs on the conjunctiva and that it is unusual for keratitis to occur as a manifestation of this condition. Can they state just what it is in this form of keratitis which is typical or characteristic of lymphogranuloma venereum?

I have recently observed 2 cases similar to the ones described in which the condition cleared up under treatment with sulfonamide drugs and a third case in which improvement followed penicillin therapy. There was no clinical evidence of lymphogranuloma venereum in any of these cases, although laboratory tests were not made.

As Dr. Henle pointed out, there are several other conditions in which the Frei test may give a positive reaction. It does seem that the authors' case in which the laboratory findings were positive can be accepted as a real case of lymphogranuloma venereum. In the others, however, the diagnosis would be presumptive.

DR WARREN S. REESE: I should like to ask whether this lesion bears any resemblance to the so-called salmon patch seen in interstitial keratitis.

DR GEORGE F. J. KELLY: Does sulfonamide therapy alter the results of subsequent Frei tests? The recurrences reported in 2 cases were thought to be due to inadequate treatment. Is there any known standard of treatment for prevention of recurrences?



DR ALAN S CRANDALL It might be interesting to show how the presumptive diagnosis was made in the last case. The patient had been seen several times, and lymphogranuloma venereum was not suspected until we examined a photograph which Dr Scheie brought back from India, showing keratitis in a patient with a condition so diagnosed. The similarity of the lesions was so striking that we immediately started to study our patient with this disease in mind.

From the evidence in these few cases, I believe that the lesion is characteristic of lymphogranuloma venereum. However, by the time the lesion becomes typical there is permanent corneal damage. There will be some scarring and vascularization, and it would be well if the index of suspicion were high enough to prompt adequate treatment before the permanent damage occurs. I should like to reiterate the importance of continuous treatment for at least three weeks. The 2 patients who did not do well did not keep up adequate therapy.

DR HAROLD G SCHEIE First I believe there is little question that the lesion discussed is primarily keratitis rather than conjunctivitis. In the 1 patient who was seen early, the onset was associated with symptoms of conjunctivitis but the corneal lesion promptly appeared. In all the cases we have discussed as well as in the case reported by Meyer and Reber, the conjunctiva seemed to show only secondary injection. There were no granulating lesions on the conjunctiva, and adenopathy was not observed.

The appearance of the corneal lesion seems characteristic of and specific for the disease. Most important is examination with the slit lamp. The cornea is involved through its entire depth. The lesion first appears within the upper portion of the limbus. In 2 of these cases a similar corneal infiltrate subsequently developed within the lower portion, which also became vascularized. The vascularization is quite characteristic. The vessels are all superficial and resemble an epaulet extending onto the cornea from the upper part of the limbus, elevating its surface. The vascularized area does not stain. The lower border of the vascularized area is sharply delimited, no isolated vessels growing into the infiltrate in front of the vascularized zone.

The patient first seen in the clinic of the Hospital of the University of Pennsylvania by Dr Crandall was presented and discussed at one of the weekly conferences of the clinic. The final conclusion reached by the staff members was that neoplasm had definitely to be excluded as a diagnostic possibility because of the new vessels and the elevation of the surface of the cornea.

Dr Reese asked what resemblance these vessels had to the "salmon patch" of interstitial keratitis. The vessels in keratitis associated with lymphogranuloma venereum are superficial rather than deep, as in interstitial keratitis.

Dr Kelly asked about the effect of sulfonamide compounds on the Frei test. It has none, and the reaction to the Frei test remains positive for life. This explains why the Frei test can be confusing and the diagnosis of lymphogranuloma venereum as the cause of any lesion must remain presumptive until the virus can be recovered.

Our last case was the most conclusive one we have had to present. The patient gave a positive reaction to the Frei test and a very strongly positive complement fixation reaction as well. Biopsy of the corneal

lesion showed changes compatible with the diagnosis of lymphogranuloma venereum, and now the virus inoculations seem to be giving positive results

Finally, I might say that none of my colleagues or I have seen this corneal lesion in any patient who did not show at least a positive reaction to the Frei test for lymphogranuloma venereum. Even so, the diagnosis is still presumptive.

**Pigmented Nevus of the Iris Treated by Iridectomy** DR JAMES S SHIPMAN and DR P ROBB McDONALD

A white woman aged 59 had had a spot on the iris of the left eye as long as she could remember. Recently it had increased slightly in size. A tumor was noted in the lower temporal quadrant of the left iris. The growth extended from about 1 mm from the pupillary margin to the iridocorneal angle. The ciliary body was not involved. The tumor was removed by iridectomy, both operation and convalescence being uneventful. A diagnosis of leiomyoma was made by Dr Perce DeLong and of nevus by Dr A B Reese. Dr Reese stated the lesion was a true nevus of the iris, since nevus cells were present.

The tumor was completely removed at operation, and when the patient was last seen vision in the left eye was correctable to 6/6.

DISCUSSION

DR PERCE DELONG. The tumor under question has been submitted to many pathologists, and varied diagnoses have been obtained. Some expressed the belief that it was malignant, others, that it was a nevus in an unusual location in the iris, and others that it was a myoma.

Nevi of the iris usually grow from the anterior surface. This neoplasm arose from the substructure. It is unusual for a nevus to develop from this location.

The microscopic picture showed no special arrangement, i. e., there was no alveolar arrangement of cells, commonly spoken of as nevoid bodies, nor did the tumor contain epithelioid cells—both common in nevus. Instead, the cells were arranged in whorls. They were long spindle cells and possessed many fibrils. Also, with the phosphotungstic acid hematoxylin stain the nuclei showed an acidophilic reaction, a characteristic common to myoma, for this reason I feel that this tumor is a neoplasm.

DR W ZENTMAYER. In 1 of 2 cases occurring in my experience the same difference of opinion existed among the pathologists. The boy had a fleshy growth of the iris, which I removed according to the technic described tonight.

The diagnosis of the first pathologist who examined the growth was leukosarcoma. He submitted it to a second pathologist, who made a diagnosis of leiomyoma. Because of this difference of opinion, it was examined by a third pathologist who confirmed the diagnosis of the first pathologist. It was later studied by Colonel James E Ash, who agreed with the second pathologist that it was a leiomyoma.

DR W E FRY. I had the opportunity of seeing Dr Zentmayer's patient at the time of operation, as well as of studying the slide after the section was prepared. The case was somewhat similar to one which I previously studied, as did Dr Adler and Dr Waite, the difference

being chiefly that in the latter a contact glass was useful in determining the presence of a free angle

I saw the slides in Dr Shipman's case and have talked to both Dr DeLong and Dr Reese, and I think there are reasons for the differences in opinion. There could be some controversy in regard to the cells. I believe that this was a tumor in which the pigment-bearing cells were important, a malignant melanoma. Certainly, the patient was properly treated.

DR BURTON CHANCE. Dr Zentmayer's case had certain aspects rather like those of a case of my own. The tumor was removed in a manner similar to that described by Dr McDonald. The patient had had all sorts of diagnoses. There had been a gradual yet appreciable growth in the previous five years. The tumor proved to be a mixed cell sarcoma. I was under stress by the patient's insistence that I should remove the eye immediately if the mass were malignant. The onus of the decision was assumed by the patient. With the assent of Drs Posey and Madison Taylor, an otherwise perfectly healthy eye was excised. That was twenty-odd years ago. Recently I learned that the patient had been in perfect health ever since the operations.

DR EDMUND B. SPAETH. I have never seen a more beautiful photograph of an eye than the one Dr McDonald showed. The photographs presented by Drs Grove and Scheie were also excellent. Presentations like these illustrate the value of good photography in recording pathologic conditions.

DR JAMES S. SHIPMAN. No less an authority than Duke-Elder states that present ideas as to the nature and classification of neuroectodermal tumors are in a state of flux. It was not until 1910 that Verocay showed that these tumors were derived from a proliferation of the cells of the sheath of Schwann, and therefore of ectodermal origin.

Masson, from 1926 to 1932, confirmed this opinion and revolutionized all previous conceptions of neuroneoplasms. His researches were also confirmed by Stewart and Copeland, in 1931, by Foot, in 1932, and by others. Masson showed that cutaneous nevi arose from a neoplastic proliferation of the specialized end organs of the cutaneous nerves, namely, the Meissner corpuscle, in the dermis, and the Merkel-Ranvier corpuscle and chromatophore, special types of cells in the basal layers of the epithelium.

As a result of these observations, according to Duke-Elder it appears that a number of tumors which used to be described in the literature as neurofibroma, plexiform neuroma, ganglionic neuroma, nevus melanoma and certain types of sarcoma are neurogenic, the fundamental cell of origin being the cell of Schwann.

According to Duke-Elder and Algernon Reese, nevi usually occur in the skin or conjunctiva or at the junction of these two structures, and they are neuroepithelial in origin, springing from the end apparatus of the sensory nerves, which may be pigmented or nonpigmented.

The term melanoma seems to have been rather loosely used to describe a pigmented tumor in any part of the body and has no real value in indicating the origin or the malignancy of the tumor. As has been pointed out in the presentation of this case, a pigmented tumor may be congenitally present in the iris for many years with no evidence

of growth or increase in size until suddenly, for some unknown reason, it takes on the characteristics of a malignant growth, as shown by its increase in size and extension into the angle of the anterior chamber, with resulting increase in the intraocular tension

Certainly, these signs should always make one suspicious of its malignant character and advise operation, as was done in this case, with the hope of removing the tumor in its entirety before it has invaded too far the angle of the anterior chamber

I feel that this case demonstrates the necessity of careful observation. Dr. Roth, who saw this patient and referred her to me, is to be congratulated on his acumen in judging the time for surgical intervention. I am indebted to him for having referred this patient to me. I am more indebted to Dr. Zentmayer, who confirmed our opinion as to the operation to be performed and who, more than that, taught me just how it should be done. I had the pleasure of being his assistant at a similar operation for just such a tumor of the iris about nineteen years ago, when I was a resident at the Wills Hospital.

This case has been presented as a preliminary report, with the hope of stimulating discussion and interest in tumors of the iris. Dr. McDonald and I hope to give a more complete report of this case at a later date, when a more definite diagnosis has been agreed on.

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#### NEW YORK ACADEMY OF MEDICINE, SECTION OF OPHTHALMOLOGY

Brittain F. Payne, M.D., *Chairman*

Milton Berliner, M.D., *Secretary*

May 20, 1946

#### INSTRUCTION HOUR

**Roentgenography in Ophthalmic Diagnosis** DR. RAYMOND L. PFEIFFER

After listing and evaluating various indications for the use of roentgen rays in ophthalmology, the author selected several conditions which afforded an opportunity for the demonstration and discussion of recent contributions of roentgenology to the study of diseases of the eye. The value of the roentgenogram in the diagnosis of retinoblastoma was considered. Deposits of calcium were found in approximately 80 per cent of a large series of cases, and calcium was observed microscopically in only an additional small per cent. Internal fracture of the orbit was demonstrated as the cause of enophthalmos in cases in which there was no external bony deformity. Intracerebral deposits of calcium as the most important diagnostic finding in toxoplasmosis were shown in a series of 9 cases, in most of which the author made clinical as well as roentgenographic examinations. The value of roentgenography in the study of exophthalmos was emphasized by his figures in a series of 200 consecutive cases, in 70 per cent of which changes were demonstrated roentgenologically. In 42 per cent of all cases the changes were diagnostic. The character of these diagnostic findings was then illustrated by the presentation of a number of cases of each.

## REPORT OF CASES

**Anomalies of the Iris** Report of Two Cases DR J J SAUERCASE 1—*Congenital malformation of the iris*

W B, aged 60, was seen on June 12, 1943, for a change of glasses. A "colored spot" had been noticed in his right eye by a member of his family about twenty years before, as far as he knew, it had not increased in size.

On examination, the right eye presented an ovoid, fairly regularly outlined, chocolate brown pigmented area on the posterior surface of the cornea from about 12 30 to 5 o'clock, extending from the limbus toward the pupillary area about 4 mm. Just inside the limbus, and measuring 0.5 mm, was a crescentic clear band, through which the normal structure of the iris could be seen. A sharply demarcated, ovoid, lighter brown area lay in the underlying iris from 2 to 4 o'clock, this did not extend to the pupillary edge of the iris, and the adjacent pupillary border was straightened vertically. No vessels were visible. The anterior chamber was of normal depth, and the two pigmented surfaces were not joined. On transillumination there was no suggestion of a tumor. Ophthalmoscopic examination failed to reveal any bulging posteriorly or other change. The left eye was normal. The last examination, on May 9, 1946, showed no change in the condition.

Melanosarcoma and cyst were ruled out and the diagnosis of congenital malformation was made. The probable pathogenesis was as follows. Atrophy of the anterior layer of the iris led to the formation of a defect, or gap, through which the pigmented layer of the iris protruded and became adherent to the posterior surface of the cornea, giving rise to the pigmented area on the cornea. This adhesion later separated from the cornea, leaving pigment on the posterior surface of the cornea.

CASE 2—*Bilateral cyst of the pigment layer of the iris*

C D, aged 45, was examined on Jan 4, 1944, for a change of glasses. In the right eye a smooth, globular brownish cystic mass was just barely visible within the temporal pupillary area from 8 to 11 o'clock, it lay behind the iris and protruded into the area anterior to the lens. The left eye presented a similar but larger mass which was also visible in the temporal pupillary area from 1 to 6 o'clock, it arose from behind the iris and protruded into the pupillary area, anterior to the lens. When the pupils were dilated, these cystic masses were more clearly visible and extended farther into the pupillary areas. On transillumination there was no interference with the passage of light. Ophthalmoscopic examination revealed nothing abnormal.

The diagnosis of bilateral cyst of the iris was made from the symmetric location, the smooth surface, the lack of vascularity, the globular shape and the absence of interference with the passage of light.

## DISCUSSION

DR ARNOLD KNAPP I was particularly interested in a feature of Dr Sauer's first case which concerns the bulging, pigmented area in a defect of the mesodermal layer of the iris. When the pupil was dilated, the iris partly covered the pigmented area and flattened it out, an

observation which did not suggest either a tumor or a cyst. In my opinion, this case belongs with malformations of the iris. Within the last few weeks the patient was seen at the Institute of Ophthalmology for a check with the drawing made in 1943, and then Dr DeVoe was able to make a gonioscopic examination, which I think will add a great deal of information to the interpretation of the case.

DR GERARD DEVOE The gonioscopic examination showed clearly that the lesion was not a cyst. The pigment on the cornea seemed to have been deposited there, having perhaps been shaken off from the pigment epithelium of the iris. The anterior layer of the iris was missing, and all that was left was the pigment epithelium, which was very thin and freely movable. It was interesting to note the difference between the appearance three years ago and that of a few days ago, in that now the pigment epithelium had become attached to the corneoscleral area.

DR RUDOLF AEBLI Would Dr Knapp enlighten us on how to account for the pigment on the posterior surface of the cornea?

DR ARNOLD KNAPP When I saw the patient, the pigment layer of the iris was bulging and in contact with the posterior surface of the cornea, I thought, therefore, that the pigment must have been deposited, just as Dr DeVoe says, and when the iris flattened down a deposit remained on the posterior surface of the cornea.

DR RUDOLF AEBLI If these two structures were in contact, what subsequently separated them?

DR ARNOLD KNAPP The separation was probably caused by the reformation of the aqueous. The adhesion could not have been very strong.

#### PAPERS OF EVENING

##### Extraction of Cataract in the Presence of Fluid Vitreous DR DANIEL B KIRBY

The author gave his concept of the cause of the development of cataract and of the change from normal gel, or viscid vitreous, to vitreous in the fluid state. He stressed the preliminary examination of the patient's eyes, in particular by means of ophthalmoscopy, slit lamp microscopy and tonometry, and the necessity of being on the alert for signs of degeneration or inflammation. In some cases it is possible to recognize the condition and to be aware of the presence of fluid vitreous before operation is begun. In certain instances, however, in which the fluid vitreous is in communication with the anterior chamber, the surgeon may not be aware of the condition until he has made his section and then has observed the fluid vitreous seep away. Sutures placed after the section are satisfactory in such cases, whereas it is important to place sutures before section if there is any likelihood that viscid vitreous will be lost. When the sutures are placed after section, the cataract is delivered by traction, rotation and stripping of the zonule, if the latter is resistant. The loop may be used to support the lens and bring it forward but should not be the only means of traction, as the zonule is not ruptured easily enough by traction alone. Pressure on the outside of the globe is contraindicated, because it is ineffective and adds to the complication. Such eyes react better to intracapsular

extraction than to capsulotomy and expression. Two short series of cases of cataract were reported in which the results in eyes in which the fluid vitreous was well contained behind the capsulozonular-hyaloid barriers were compared with results in eyes in which the fluid vitreous was in communication with the anterior chamber. Satisfactory results were obtained with observance of the surgical principles outlined.

#### DISCUSSION

DR WATSON GALEY, Bloomington, Ill. I am sorry that Dr Kirby did not discuss the conservation of viscid vitreous during the course of cataract extraction. I am always apprehensive about the spilling of vitreous, whether viscid or fluid, but I think I manage my cases with fluid vitreous much better than I do those with viscid vitreous. The "fish mouth" wound which follows immediately after delivery by the intracapsular method is very annoying and distressing.

DR ARNOLD KNAPP. I should like to emphasize two points in Dr Kirby's interesting paper. First, in my judgment, it is a mistake not to put in preliminary sutures before operating if there is any opportunity for loss of vitreous. Second, if fluid vitreous is encountered, an iridectomy should always be done. In the presence of prolapse of the vitreous the question arises: How fluid is the vitreous, and how great is the subluxation of the lens? I should like to remind the members of the Section of a method suggested by Dr Herman Knapp many years ago by which he was able to extract the dislocated lens by manipulation with external pressure. This method may be considered when the vitreous is thick. In recent years the late Dr Jameson published a similar procedure. In cases in which there is a fairly normal vitreous the lens will frequently return into position after a few days and thus facilitate the extraction. To fish for a completely dislocated lens in fluid vitreous is very hazardous. Van der Hoeve suggested a procedure through which by placing a suture under the insertion of each of the rectus muscles and by pulling on the sutures the eye was drawn forward and no pressure could be exerted on the sclera.

DR JOHN McLEAN. Dr Kirby's paper does not leave much room for discussion, but there are a few points on which I should like to hear him comment further. One is the argument over retrobulbar injection. Inasmuch as retrobulbar injection tends to soften the globe and it is a simple principle of hydrodynamics that fluids do not flow uphill, so that vitreous to flow out of the eye must be pushed out either by the patient or by the surgeon, is it not worth while, particularly with fluid vitreous, to use retrobulbar injection as a routine, in order to make it harder for the patient and the surgeon to push the vitreous out?

I do not quite follow Dr Kirby's reasoning about not using preplaced corneoscleral sutures when fluid vitreous is present or is suspected. Not long ago I watched with some horror one of the strong advocates of placing sutures after section practically wallowing in vitreous, which had escaped immediately after the section, while he wasted time and vitreous in getting down to the fundamental business of dealing with the lens and the vitreous, and I felt he would have saved time, effort and vitreous if his sutures had been there before the eye was opened.

The third point on which I should like to hear Dr Kirby comment is his choice of delivery of the lens in a case of fluid vitreous by grasping it above, when it would seem that a somewhat better barrier to premature loss of vitreous would be provided by dislocating the lens below first, grasping it below and tumbling it, so that the zonule is left as intact as possible above.

DR PURMAN DORMAN, Seattle. Some of my fellow ophthalmologists and I have become accustomed to making a keratome incision for cataract extraction. If fluid vitreous is anticipated, a preliminary canthotomy is done. We have always admired the smoothness of the linear knife incision as done by Dr Kirby. Skill even approaching his is not always maintained. The keratome incision may be better placed by those of us who are less deft. Perhaps Dr Kirby will comment on this habit of ours of using the keratome incision and the preliminary canthotomy.

DR RUDOLF AEBLI. My own experience is that when the vitreous has been lost my preparation has been inadequate. I have come to the conclusion that a perfect akinesia, with an external canthotomy and injection of the muscle cone, is the best guaranty against loss of vitreous.

DR DANIEL B. KIRBY. I appreciate the discussion. There is great interest in any phase of cataract surgery, particularly in the problem of loss of vitreous.

Dr Gailey, the matter of viscid vitreous opens up a whole new chapter. I should like to study the problem for a year or two before I talk about it further.

I appreciate Dr Knapp's discussion. He has had great experience and is very wise in his surgical treatment. I should always do an iridectomy if there was viscid or semifluid vitreous in the wound, but I have seen cases in which the results were very good with what is called completely fluid vitreous. I have not had experience with Verhoeff's technic, but it sounds logical.

Dr McLean, I do not believe that retrobulbar injection always softens the eye. I have given up retrobulbar injection except with the younger patients, who have good vessels. I have seen cases in which extravasation of fluid and blood into the orbit pushed the eye forward.

Dr Dorman mentioned external canthotomy. I used to do many canthotomies before I gave up retrobulbar injections.

Dr McLean says that vitreous will not flow out but has to be pushed out. I do not believe that is true in regard to fluid vitreous, for there is the weight of the sclera and of the surrounding tissues and the effect of their collapse on the fluid vitreous. I am sure that in the cases I reported I was not pushing the fluid vitreous out.

The question of preplaced sutures requires separate discussion. I am in accord with Dr McLean on the value of sutures in cases of viscid vitreous, but I should not place them in every ordinary case. The mode of inserting them by the average surgeon often results in more trauma than it should. They are often in the way. There are many advantages in grasping the capsule above. I do not like to grasp it below, particularly in a case of fluid vitreous in which the lens drops back to the posterior position. One cannot see what one is doing unless the corneal flap is raised. I have never seen any bad results from raising the corneal flap. I believe it is a most conservative procedure. I do the iridectomy



and place the lens capsule forceps under direct view. If the surgeon must place a forceps below when the lens is far posterior and must reach well in to pick it up, there is not the chance of completing the operation as satisfactorily as when the capsule is grasped above.

I do not see any reason for the recent trend to use of the keratome. Unless there is some complication, the Graefe knife is very satisfactory, and there is no reason for not adhering to its use. It gives a cleaner section and less trauma at the beginning of the operation. It is necessary to make less section with the scissors. In a letter which I received from Traquair the other day, he said that he relied on anesthesia, complete local anesthesia, rather than on akinesia. I think that both are important, Dr. Aebli, and that you are right about careful preoperative preparation in avoiding complications. I do not pretend to know much about the matter of viscid vitreous.

### **Onchocerciasis in Guatemala. A Preliminary Report** DR. WILLIAM B. CLARK, New Orleans

I was invited to participate in a study of onchocerciasis in Guatemala in 1945 by the Pan-American Sanitary Bureau. The investigation was carried out in Yepocapa, a village of 8,000 inhabitants in the Department of Chimaltenango. A study of the insect carriers and the habits of the *Onchocera volvulus* revealed that man is the true host and that the parasites are picked up by a fly of the genus *Simulium* when it bites. After maturity, the parasites enter the proboscis of the fly, where they are ready to reenter the host when the fly pierces the skin. The larvae then migrate through the subcutaneous tissue until they find a suitable place to make a nodule. It is from the nodules that adult worms can be taken. All stages of development may be seen, from the egg to the microfilarias breaking out of the shell. The average size of the microfilarias is about 8 by 300 microns, so the larva must be magnified about twenty-two times for it to be seen in the anterior chamber and for the details of its movements to be visible.

My colleagues and I reexamined 1,215 patients known to have, or suspected of having, onchocerciasis. A complete ophthalmic examination was made of each patient. In addition, biopsies of the skin and conjunctiva were done. In all cases in which biopsy showed positive changes in the conjunctiva or an aqueous flare was seen, we did a paracentesis and examined the aqueous under the microscope.

Of 62 of these patients, the aqueous of 29 showed the presence of two or more microfilarias. We also did a paracentesis on several patients who complained of entoptic vision but who had no positive changes in the conjunctiva, and in no case did we find microfilarias in the aqueous. Another remarkable observation was that none of the 29 patients from whom we recovered the microfilarias from the anterior chamber complained of entoptic vision. To me, the most striking features were the anterior chamber literally filled with microfilarias without injection of the eye and the changes produced in the cornea and iris by this infection without ciliary injection.

Of the 1,215 patients examined, 967 had nodules or had previously had nodules removed. The prevalence of nodules, the results of biopsy of the skin and conjunctiva and of paracentesis, and the lesions of the cornea, iris and fundus are tabulated.

Only one eye was obtained for pathologic study, which has not been completed. The eye was removed because of the pain associated with an attack of secondary glaucoma.

## DISCUSSION

DR BERNARD FREAD: What measures are taken by travelers to Guatemala to avoid getting this disease?

DR ALGERNON REESE: What is the treatment for the disease?

DR WILLIAM B. CLARK, New Orleans: I do not think that an occasional bite from the simulum is dangerous. I had several bites on my bald head while making this study and the members of my brigade were also bitten, and in none of us did nodules develop. The ordinary insect repellent used by the armed forces keeps the flies away. We used this in the beginning, but, as always, we became careless toward the end and left it off until we got a bite. The bite is quite painful and stings for a few minutes, and it usually leaves a red wheal, which may persist for several hours. Many of the managers of the coffee *fincas* are of Swiss or German extraction, and some of them have lived in the zone as long as forty years without becoming infected. However, occasionally some one other than an Indian will appear with the infection.

Removal of the tumors after they occur is the accepted form of treatment, but in my opinion this is of questionable value. Part of our project was to try certain new drugs sent down by the Institute of Health, but the physician who was to administer them was transferred and the situation caused by his leaving was not cleared up by the time we had completed our ophthalmic survey. I hope that before we make a final report on this subject we shall have information on the response of the microfilarias to drug therapy.

## Book Reviews

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Archivos de la Asociación para evitar la Ceguera en Mexico  
(Archives of the Association of Prevention of Blindness in Mexico) Vol III, Pp 282 Mexico, 1945 Director, Dr L Sanchez Bulnes, Editor, Dr Daniel Silva Gomez Farias Num 19, México, D F

The book begins with a report of the work done in the hospital of this association in Mexico, D F, during 1944 and a description of the activities in the various departments. Then follow a number of articles, the longest and most important is the one on "Ocular Onchocerciasis in Chiapas" by Amselmo Fonte Barcena. The author gives a history of the ocular complications of onchocerciasis reported since 1916 when Robles described them for the first time. The ocular symptoms are dominated by photophobia and blepharospasm, which in some cases are so severe that the patient cannot open his eyes at all. Besides photophobia, the patient complains of burning and a sensation of a foreign body in the eyes. These symptoms occur in attacks and disappear gradually when the infected nodules are removed.

The ocular findings vary with the acute and chronic stages of the disease. In the acute form there is pronounced, red edema of the face, more conspicuous in the lids and cheeks, which Robles termed "erysipela of the coast". The eye itself shows ciliary and conjunctival congestion, chemosis and increased fine, superficial vascularization of the tarsal and bulbar conjunctiva.

In the chronic forms the ocular signs are reduced mainly to vascularization, pigmentation and edema of the conjunctiva. The vascularization takes place in the conjunctival and ciliary vessels, nasal and temporal to the cornea in a triangular area, it fades gradually toward the periphery. The pigmentation is brown in color, pericorneal, located nasally and temporally and appears as a fine dusting of the conjunctival epithelium.

The severity of the ocular symptoms mentioned here has no relation to the local changes. Barcena expressed the belief that they are due to a toxic substance produced by the adult parasite at the time of birth of the microfilarias and, to a lesser degree, to the presence of the latter. He advanced the hypothesis that the substance produced by the parasite is a derivative of the porphyrin.

The other articles treat of motility of the intraocular cysticercus, blindness caused by quinine, injections of hypertonic solution of sodium chloride in treatment of detachment of the retina, importance of ophthalmic examinations in cases of cranial injuries, use of anesthesia in the cataract operation, contact lenses, tuberculosis of the choroid, clinical applications of angioscotometry, vegetative innervation of the visual apparatus and new instruments for dacryocystorhinostomy. Then there are four articles by authors from the United States. Obituaries of Dr Rafael Silva and of Dr Sanford R Gifford conclude the volume.

H ESCAPINI

# Directory of Ophthalmologic Societies \*

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President Dr P Baillart, 66 Boulevard Saint-Michel, Paris, 6<sup>e</sup>, France  
Secretary-General Prof M Van Duyse, Universite de Gand, Gand, Prov Ost-flandern, Belgium

All correspondence should be addressed to the Secretariat, 66 Boulevard Saint-Michel, Paris, 6<sup>e</sup>, France

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Secretary Dr Ehlers, Jerbanenegade 41, Copenhagen, Denmark

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Place Habana, Cuba Time February 1948

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Place Eye, Ear, Nose and Throat Hospital, Chengtu, Szechuan, China

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Secretary Dr C K Lin, 180 Hsi-Lo-yen Chienmeng, Peiping  
Place Peiping Union Medical College, Peiping Time Last Friday of each month

\* Secretaries of societies are requested to furnish the information necessary to make this list complete and keep it up to date

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 All correspondence should be addressed to the Assistant Secretary

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 Place Manchester, Leeds, Newcastle-upon-Tyne, Liverpool, Sheffield and Bradford,  
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 Secretary Dr Mohammed Khalil, 4 Baehler St, Cairo  
 All correspondence should be addressed to the secretary, Dr Mohammed Khalil

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 Place London Time May 30-June 1-2, 1946

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 Place H B A Free Ophthalmic Hospital, Parel, Bombay 12 Time First  
 Friday of every month

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 Secretary Dr Evaldo Campos, R Rodrigo Silva 7-1° andar, Rio de Janeiro, Brazil  
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 Secretary Dr William F Keim Jr, 15 Washington St, Newark 2  
 Place 91 Lincoln Park South, Newark Time 8 45 p m, second Monday of each month, October to May

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 Place Massachusetts Eye and Ear Infirmary, 243 Charles St, Boston Time 8 p m, third Tuesday of each month from November to April, inclusive

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 Secretary-Treasurer Dr Linley C Happ, 124 Waterman St, Providence  
 Place Rhode Island Medical Society, Library, Providence Time 8 30 p m,  
 second Thursday in October, December, February and April

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 Secretary Dr Fred Reese, 330 N Charles St, Baltimore 1  
 Place Medical and Chirurgical Faculty, 1211 Cathedral St Time 8 30 p m,  
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 Secretary Dr W Chunn Parsons, 425 Woodward Bldg, Birmingham, Ala  
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 Place Kings County Medical Society Bldg, 1313 Bedford Ave Time Third  
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 from October to May

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 Secretary Dr Mercer G Lynch, 1018 Maison Blanche Bldg, New Orleans  
 Place Louisiana State University Medical Bldg Time 8 p m, second Tuesday  
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 Secretary Dr William Mussil, Medical Arts Bldg, Oklahoma City  
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 tember to May

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 Secretary-Treasurer Dr W Howard Morrison, 1500 Medical Arts Bldg, Omaha 2  
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 program, third Wednesday of each month from October to May

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 Secretary-Treasurer Dr J Averbach, 435 Clifton Ave, Clifton, N J  
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 from September to July

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 to April, inclusive, except December, at 8 00 p m

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## PHYSIOLOGIC FACTORS IN DIFFERENTIAL DIAGNOSIS OF PARALYSIS OF SUPERIOR RECTUS AND SUPERIOR OBLIQUE MUSCLES

FRANCIS HEED ADLER, M D  
PHILADELPHIA

AN ARTICLE by Davis<sup>1</sup> on the differential diagnosis of paralysis of a superior oblique muscle and paralysis of the opposite superior rectus muscle has revived the argument between Bielschowsky and Duane as to the relative frequency of these paralyses, the former believing that most vertical anomalies are due to paralysis of the superior oblique, while the latter credited the superior rectus with the majority. Davis found the superior oblique paretic in 54.5 per cent of 88 cases of vertical anomalies and the superior rectus in 45.4 per cent. White and Brown<sup>2</sup> had previously reported that only 4 per cent of cases of vertical anomalies were due to paralysis of the superior oblique and that 96 per cent were due to paralysis of the superior rectus. Smith<sup>3</sup> recently pointed out the serious discrepancy between these two sets of figures and pleaded for a more uniform standardization of methods of diagnosis.

Such a discrepancy in figures must be due to the employment of different criteria in diagnosing paralysis of a vertically acting muscle or to differences in the type of case analyzed by different authors. The classic signs of paralysis of each of these muscles should enable one to make a positive diagnosis unless factors not generally recognized arise and make the diagnosis difficult. In the usual textbook picture the following signs are so characteristic that one should be able to make a positive differential diagnosis when they are present.

1 The head is tilted. This is the most characteristic sign of paralysis of a superior oblique muscle, and, although it occurs to a lesser degree with paralysis of a superior rectus muscle, it is pronounced only with

From the Ophthalmological Department of the University of Pennsylvania School of Medicine.

Read at the Eighty-First Annual Meeting of the American Ophthalmological Society, Hot Springs, Va., Nov. 12, 1945.

1 Davis, W. T. Paresis of Right Superior Oblique and of Left Superior Rectus Muscle, *Arch. Ophth.* **32**: 372-380 (Nov.) 1944.

2 White, J. W., and Brown, H. W. Occurrence of Vertical Anomalies Associated with Convergent and Divergent Anomalies, *Arch. Ophth.* **21**: 999-1009 (June) 1939.

3 Smith, J. W. Paresis of Right Superior Oblique and of Left Superior Rectus Muscle, *Arch. Ophth.* **33**: 77 (Jan.) 1945.

paralysis of one of the oblique muscles. The reason for this may be stated as follows:

When the eyes are in the primary position, a paralysis of one of the oblique muscles produces a marked tilting of the vertical meridian of the affected eye and little up or down displacement. Figure 1 shows that the superior oblique muscle is 100 per cent effective in depressing the globe only when the eye is adducted 51 degrees. Since the effectiveness of a muscle in producing any particular movement of the globe changes from zero to 100 per cent through a rotation of 90 degrees, each degree represents an increase in effectiveness of 1.1 per cent from the

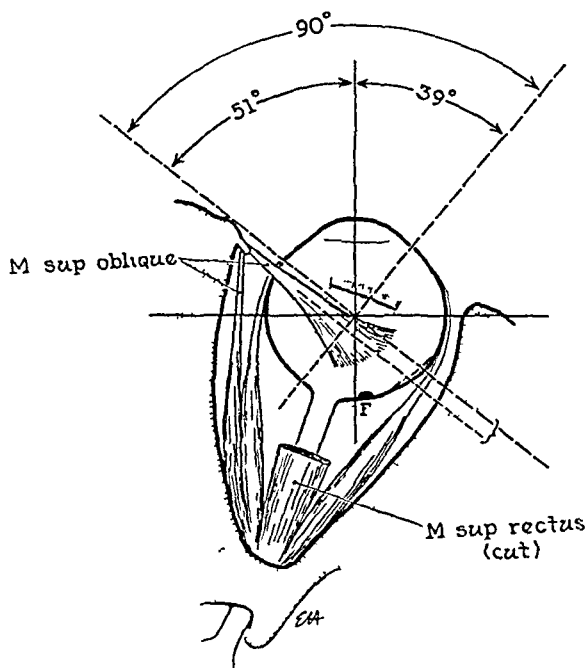


Fig. 1—Effectiveness of the superior oblique muscle in depressing the globe when the eye is adducted 51 degrees.

zero position. In the primary position, the effectiveness of the superior oblique muscle as a depressor is 42.9 per cent, and its effectiveness as an intorter is 56.1 per cent.

When these figures are compared with those for the superior rectus (fig. 2), it is evident that in the primary position this muscle is 73.7 per cent effective as an elevator and only 25.3 per cent effective as an intorter. What has been said of these two muscles is equally true of the inferior oblique and inferior rectus muscles.

The response on the part of the body to a paralyzed ocular muscle is to compensate as far as possible for the disturbing effects of the diplopia produced. This can be accomplished either by suppressing the image of one eye or by holding the head in such a position that the diplopia is

abolished or lessened The position of the head, which is the present concern, is determined by the action the paretic muscle has in the primary position of gaze

In the case of paralysis of an internal rectus or an external rectus muscle the head is simply turned toward one or the other shoulder, since these muscles have no action other than horizontal rotation The superior and inferior rectus muscles and the oblique muscles, however,

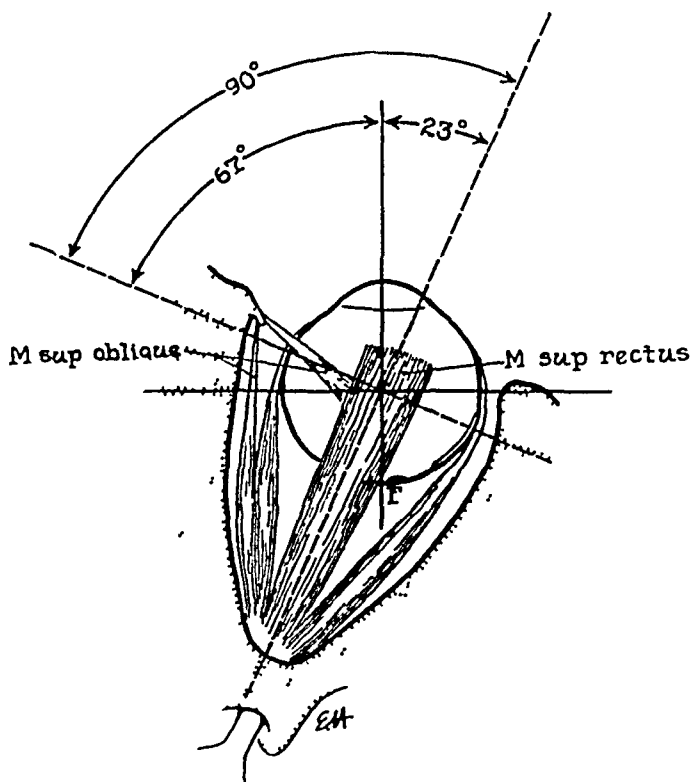


Fig 2—Effectiveness of the superior rectus muscle as an elevator and as a depressor

*Effectiveness of Rectus and Oblique Muscles in Primary Position*

| Muscle           | Intorsion or<br>Latorsion, % | Elevation or<br>Depression, % |
|------------------|------------------------------|-------------------------------|
| Superior rectus  | 25.3                         | 73.7                          |
| Inferior rectus  |                              |                               |
| Superior oblique | 56.1                         | 42.9                          |
| Inferior oblique |                              |                               |

have both vertical action and torsion in the primary position of gaze by the amounts just estimated (table) The head must be moved, therefore, in such a manner as to compensate as far as possible for both these components (I have purposely left out the abducting and adducting actions of these muscles because they do not seem to me to be theoretically correct as usually given The superior rectus, for example, is called an adductor, which is true in the primary position As the eye is turned

nasalward, the adducting power should increase, but as it is turned temporally and beyond 23 degrees the action should change to abduction. Besides this, the lateral phorias may so alter the final picture in the horizontal, when the eyes become dissociated, that it would only confuse the issue to take this action into account here.)

The vertical component can be compensated by elevating or depressing the chin. The torsional component must be taken care of by tilting the head on one or the other shoulder. It was first shown by Nagel in 1871<sup>4</sup> that when the head is tilted on the shoulder the vertical meridians of the corneas remain vertical and do not tip as the head tilts. It is now well known that the muscles controlling torsion are under the influence of tonic impulses from the otolith apparatus and that when the head is tilted on one shoulder the vertical meridian of the eye on that side is intorted to keep it vertical and the vertical meridian of the opposite eye is extorted to keep it vertical. If the head is tilted on the right shoulder, for example, the muscles which intort the right eye (superior rectus and superior oblique) contract, and the muscles which extort the vertical meridian of the left eye (inferior rectus and inferior oblique) contract. In this way the vertical meridians are kept upright.

If a muscle which produces torsion in the primary position is paralyzed the vertical meridian of that eye will be tilted and will not be parallel to the vertical meridian of the opposite eye. In order to avoid this tilt, as well as the vertical deviation which occurs (if the superior oblique is paralyzed, the eye will be extorted and higher than the opposite eye, owing to the unopposed tone of the inferior oblique and the compensating pull of the superior rectus of the same side), the head will be held in that position which brings the vertical meridian of the normal eye parallel with that of the paralyzed eye. This is accomplished by tilting the head on the opposite shoulder. In this position the intorters of the sound eye and the extorters of the paralyzed eye are contracted. The intorters of the paralyzed eye are relaxed, hence, in a paralysis of the superior oblique muscle the vertical meridians are brought into parallelism by tilting the head on the opposite shoulder, and the up and down deviation is kept at a minimum.

Tilting of the head is therefore marked and is diagnostic of paralysis of an oblique muscle. It does occur with paralysis of a superior rectus muscle, but to much less extent.

2 The head is always tilted to the side opposite the paralyzed muscle. For example, in a case of right hypertropia due to paralysis either of the right superior oblique or the left superior rectus, if the right superior

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<sup>4</sup> Nagel, A. Ueber das Vorkommen von wahren Rollungen des Auges um die Gesichtslinie, Arch f Ophth **17** (pt 1) 237, 1871

oblique is at fault, the head will be strongly tilted toward the left shoulder, if the left superior rectus is at fault, the head will be slightly tilted toward the right shoulder

3 A third means of differentiation, which is to be found in cases of both recent and old paralysis of an oblique muscle, but is never present with paralysis of the vertical rectus muscles, is the vertical movement of an eye with a paralyzed oblique muscle when the head is tilted by the examiner on the shoulder of the same side as the paralyzed eye. If the right superior oblique is paralyzed and the head is tilted on the right shoulder, the right eye will be seen to make a definite upward movement. Bielschowsky<sup>5</sup> called attention to this sign, and he and Davis stressed the subjective phenomena which accompany it, i.e., the increase in the vertical diplopia. Since the majority of patients with vertical motor paralysis are children, who frequently suppress with one eye, diplopia fields often cannot be taken, and the objective sign is therefore of much more value.

The pathologic physiology which produces this vertical movement is as follows. Tilting the head on the right shoulder sends an increase of tonic impulses to those muscles of the right eye which cause intorsion, i.e., the right superior oblique and the right superior rectus. Normally these two muscles, contracting together by just the right amount, produce nothing but intorsion, as their elevating and depressing actions on the globe neutralize one another. If the right superior oblique is paralyzed, the superior rectus works alone and produces some intorsion but also a marked elevation of the globe, since its upward movement is no longer prevented by the forward pull of the superior oblique muscles.

If the superior rectus is paralyzed and the head tilted on the shoulder of the same side, no upward movement of the globe is produced, since the muscle which is most effective in producing intorsion is still intact (superior oblique). The necessary amount of intorsion is produced by this muscle practically alone, the superior rectus being contracted simultaneously merely to counterbalance the slight depressing action of the superior oblique as it contracts in the primary position. If any vertical movement of the globe results from this tilting procedure it will be a slight downward movement of the eye, due to the unopposed action of the superior oblique.

On the basis of these facts, one should be able to differentiate between a paralysis of the superior oblique and a paralysis of the superior rectus of the opposite side by the following criteria:

1 One eye will be higher than the other when the eyes are in the primary position, i.e., there will be right or left hypertropia. If the

<sup>5</sup> Bielschowsky, A. Lectures on Motor Anomalies, Hanover, N. H., Dartmouth College Publications, 1940.

paralysis is of the superior oblique muscle, it will be on the side of the higher eye. If the paralysis is of the superior rectus muscle, it will be on the side of the lower eye.

2 If the patient habitually carries the head tilted on the shoulder of the side of the higher eye, the muscle paralyzed will be the superior rectus of the opposite eye. The tilting of the head will probably not be pronounced. If the head is habitually tilted on the shoulder of the side of the lower eye, the paralyzed muscle is the opposite superior oblique. The tilting of the head will generally be pronounced.

3 If the examiner, having decided which eye has the paralyzed muscle, tilts the patient's head to the shoulder of the same side as the paralyzed eye, this eye will be seen to make an upward movement if the superior oblique is paralyzed but will not move upward if the superior rectus is paralyzed. If any vertical movement occurs it will be a slight downward movement.

These diagnostic signs hold only for unilateral paralyses. They are of no value in cases of bilateral paralyses. They are diagnostic in cases of primary vertical motor paralyses, usually congenital, but there is doubt as to their value in cases of so-called secondary vertical motor paralyses, i. e., those cases of convergent squint associated with an incomitant vertical deviation. The type of paralysis I have in mind is generally reported as a convergent squint associated with an overaction of one or both inferior oblique muscles. It seems probable that the explanation of the discrepancy between Davis' statistics and those of White and Brown is that the latter authors were basing their opinion of the frequency of paralyses of the superior rectus on statistics of cases of the latter type, whereas Davis had in mind the isolated primary vertical motor paralysis. In my experience, an isolated primary vertical motor paralysis is most commonly due to paralysis of the superior oblique, and isolated paralyses of the superior rectus are rare and nearly always associated with ptosis. On the other hand, the vast majority of the cases of secondary vertical motor paralyses more nearly fit into the picture of paralysis of a superior rectus. In all such cases in which I have applied the diagnostic tests just outlined the paralysis acts more like one of the superior rectus. In these cases the tilt of the head is never marked, nor does either eye move upward when the head is tilted by the examiner on either shoulder. In this respect I agree with White and Brown, but it seems to me the evidence is still too scant to justify a positive assertion that there is or has been a paralysis of the superior rectus in these cases. The nature of the paralysis is still far from clear.

One frequently sees statements in the literature that when a muscle is paralyzed its antagonist overacts and then undergoes contracture or shortening. Chavasse<sup>6</sup> made the following statements, for example

If the external rectus becomes paretic the internus eventually becomes shortened. It overacts. . . if the left superior oblique is paretic there follows contracture and overaction of the inferior oblique (direct antagonist). This may persist even if the original palsy is no longer clinically demonstrable.

Contracture of a muscle does occur in cases of severe paralysis if the condition is of long standing, but the use of the term "overaction" should not be used here but should be limited to what is true overaction of a yoke muscle. When an external rectus muscle is paralyzed, the eye may become convergent in the primary position, owing to the normal tone of the internal rectus, which eventually leads to a shortening or contracture of this muscle. This muscle is not overacting. The same thing is true of the inferior oblique in cases of paralysis of the superior oblique. When a superior oblique is paretic, the inferior oblique is not opposed by its normal tone, and so the eye may be elevated, owing to contracture of this muscle. This is quite different from the true overaction of the inferior oblique when the superior rectus of the opposite eye is paretic and both eyes are turned up and to the side of the paretic superior rectus. This overaction is due to the well known law of Hering that all willed ocular movements are brought about by an equal innervation to the muscles of the two sides. If one side is abnormally weaker than the other, the amount of nervous energy which will be sent equally to the two sides is that which is just sufficient to complete the movement in the weaker of the two sides. Hence, when there is paresis of a muscle, an excessive amount of innervation must be sent to it, and, accordingly, the yoke muscle will receive an excess innervation and will therefore overact. The inferior oblique may move the eye too far as the eye is adducted because of (1) lack of opposing tone of its paretic antagonist, i e., the superior oblique of the same side, and (2) overaction due to paralysis of its yoke muscle on the opposite side, i e., the opposite superior rectus.

Another factor may so camouflage a paralysis of the superior oblique that it resembles a paralysis of the superior rectus of the opposite side. This is the phenomenon known as inhibitional palsy of the contralateral antagonist. So far as I know, Chavasse first called attention to this, and he alone has cautioned against mistaking it for paralysis of a superior rectus muscle.

In cases of paralysis of the superior oblique in which there is tilting of the head the patient may choose to fix either with the higher (para-

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6 Chavasse, F. B. *Worth's Squint or the Binocular Reflexes and the Treatment of Strabismus*, ed 7, Philadelphia: P. Blakiston's Son & Co., 1939.



lyzed) eye or with the lower (sound) eye. According to Chavasse, if the patient habitually fixes with the sound eye, inhibitional palsy will never occur, but if he habitually fixes with the paralyzed eye then the sound eye will show a limitation of movement when looking up and to the sound side. If there is a paralysis of the right superior oblique, for example, and the patient habitually fixes with this eye, then on his looking up and to the left the left eye will not move up as far as normally. This will simulate a paralysis of the left superior rectus muscle.

The physiologic basis of this phenomenon is probably as follows. The patient is fixing with his paralyzed right eye. The right inferior oblique is not opposed by a normal tone from the paretic right superior oblique. Therefore, less nervous impulse is needed to elevate the eye in levoversion than is normally required. The yoke muscle of the right inferior oblique, i. e., the left superior rectus, gets less than the required amount of stimulation, which therefore prevents the left eye from moving up as far as the right eye, in other words, an underaction of the superior rectus exists by virtue of understimulation, just as overaction of a yoke muscle may be due to overstimulation.

The importance of this feature in a case of paralysis of a superior oblique muscle is evident. The following case of paralysis of the left superior oblique was first diagnosed as one of paresis of the right superior rectus muscle, before it was recognized that the underaction of the latter was due to inhibitional palsy.

*CASE 1—Diagnosis Primary paralysis of left superior oblique, inhibitional palsy right superior rectus*

J. Y., a boy aged 11, was admitted July 20, 1943, with a history of tilting the head to the right shoulder since early childhood. The motility of the neck was free, and there was no evidence of any motor weakness or contracture of the muscles of the neck.

Visual acuity with the best correction was 6/20 in the right eye and 6/6 in the left eye. There was considerable anisometropia, the right eye having a hypermetropia of 2.50 D, while that of the left eye was corrected with a +0.37 D cylinder, axis 35.

Fixation was carried out with the left eye, the right eye being deviated downward, and the right eye failed to move much above the midline on the patient's looking up and to the right. A tentative diagnosis of ocular torticollis due to paralysis of the right superior rectus muscle was made.

At first, diplopia fields showed no double vision in any direction of gaze, but this was due to the fact that the child constantly suppressed the image of the right eye. Later, diplopia fields showed a vertical diplopia, with the lower image corresponding to the left eye. The greatest separation of the images occurred on looking down and to the left. Ophthalmoscopic examination revealed no pathologic condition, and form and color fields were normal.

On the synoptophore, his objective measurements were as follows: esotropia, 4 degrees, left hypertropia, 13 degrees. There were rapidly alternating fixation

and momentary fusion at the objective angle. No fusion occurred at zero. The patient tended to suppress with the right eye but showed alternating fixation when stimulation was given.

Screen and parallax tests showed that the greatest separation of the visual axes occurred on looking down and to the left. In this position the right eye

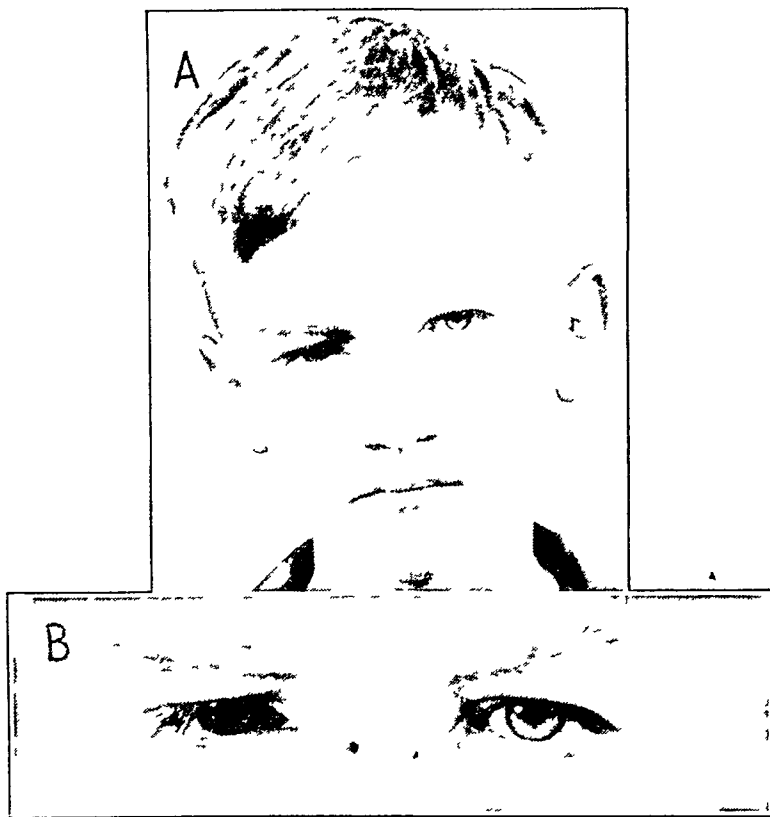


Fig 3—*A*, photograph of patient showing the head tilted to the right shoulder and fixation carried out with the left eye, which is the higher. *B*, closer view, showing the left hypertropia and fixation with the left eye. The picture was taken with the patient looking directly into the camera, i. e., at the reader's one eye.

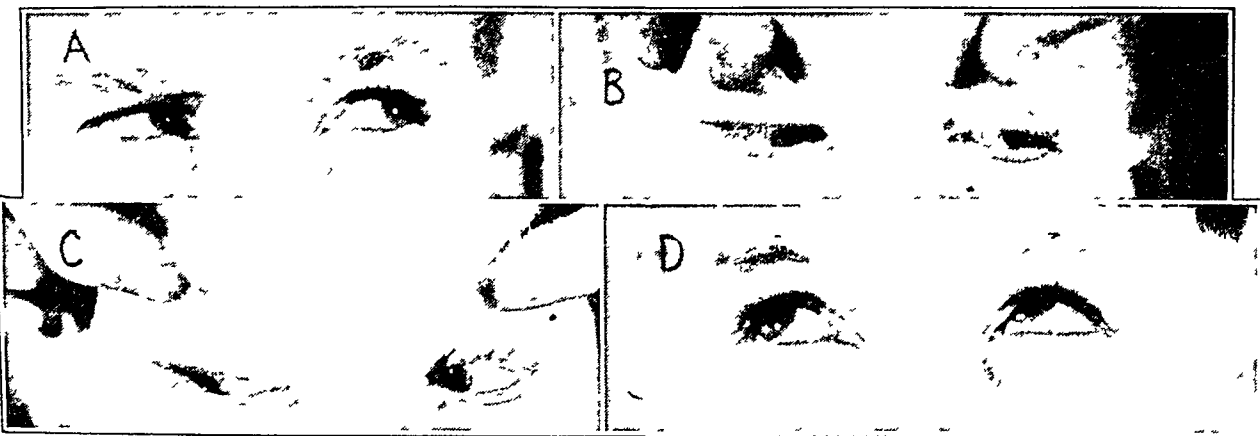


Fig 4—*A*, no deviation of the visual axes on looking up and to the left. *B*, no deviation on looking down and to the left. *C*, greatest deviation of the visual axes on looking down and to the right. The right eye moves down fully, while the left eye fails to do so. *D*, patient looking up and to the right, showing how the right eye fails to go up completely, owing to inhibitional palsy, while the left eye moves up completely.

moved down fully, while the left eye failed to follow down. In addition, however, there was a pronounced lag of the right eye on looking up and to the right, as already mentioned, so that in this position also the left eye was the higher.

Two diagnoses were possible: (1) paralysis of the right superior rectus, which could account for the failure of the right eye to move up and to the right, and (2) paralysis of the left superior oblique. The latter seemed likely in view of the failure of the left eye to move down when the gaze was directed down and to the right.

A final diagnosis of paralysis of the left superior oblique muscle was made on the following evidence, as outlined in the paper:

1. There was a decided tilt of the head to the patient's right shoulder. This is in keeping with paralysis of the left superior oblique. If the right superior rectus had been paralyzed, the head would have been tilted to the left shoulder, and the tilt would not have been so marked.

2. The patient habitually fixed with the paralyzed eye, i. e., the left, as the right eye was partially amblyopic. On his looking to the right and up, therefore,

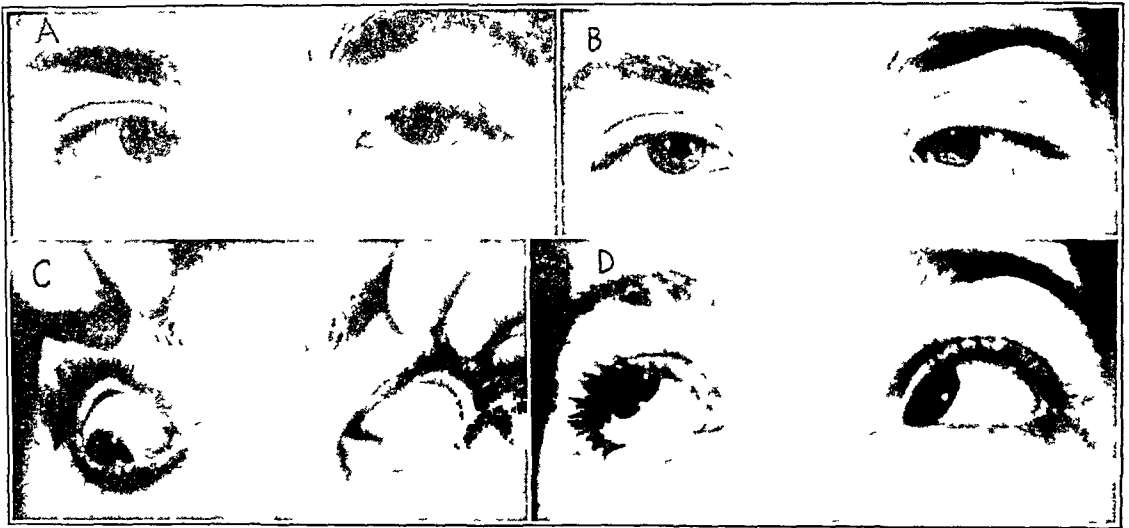


Fig 5—A, no vertical deviation when the patient is fixing with the left eye. B, depression of the left eye 8 degrees when the patient is fixing with the right eye (paretic inferior rectus muscle). C, greatest vertical deviation when the patient is looking down and to the right. The right eye fails to move down normally (palsy of the right inferior rectus), and the left eye moves down too far (over-action of the left superior oblique). D, patient looking to the right and up. The left eye fails to move up as far as the right owing to inhibitional palsy of the left inferior oblique muscle.

the left inferior oblique muscle had no opposition from the paralyzed left superior oblique and required less than the normal amount of innervation to accomplish its purpose. This lack of innervation to the muscles which turn both eyes up and to the right resulted in insufficient innervation of the right superior rectus to carry this eye up. The result was apparent paralysis of the right superior rectus.

**CASE 2—Diagnosis:** *Alternating convergent squint with secondary paralysis of right inferior rectus muscle and inhibitional palsy of left inferior oblique.*

D. P., a girl aged 15, was admitted on March 6, 1945 with a history of having had a convergent squint as long as could be remembered. Visual acuity was equal

in the two eyes with correction of a moderate amount of hyperopia and was normal

The convergent alternating squint measured 25 degrees at 6 meters without correction and was slightly less with glasses. When the patient was fixing with the right eye, the left eye turned down about 8 degrees in the primary position. The downward deviation of the left eye was greatest on looking down to the right. Although the right eye could be moved down and to the right, rotation of the right eye in this direction was not quite so complete as the corresponding movement of the left eye down and to the left. A tentative diagnosis of paresis of the right inferior rectus with partial recovery was made. This had resulted in an overaction of the left superior oblique muscle when the eyes were turned down and to the right.

When the patient was fixing with the right eye, the left eye lagged behind on looking up and to the right, indicating weakness of the left inferior oblique muscle. It was decided that this was an inhibitional palsy, and not a true paralysis, on the

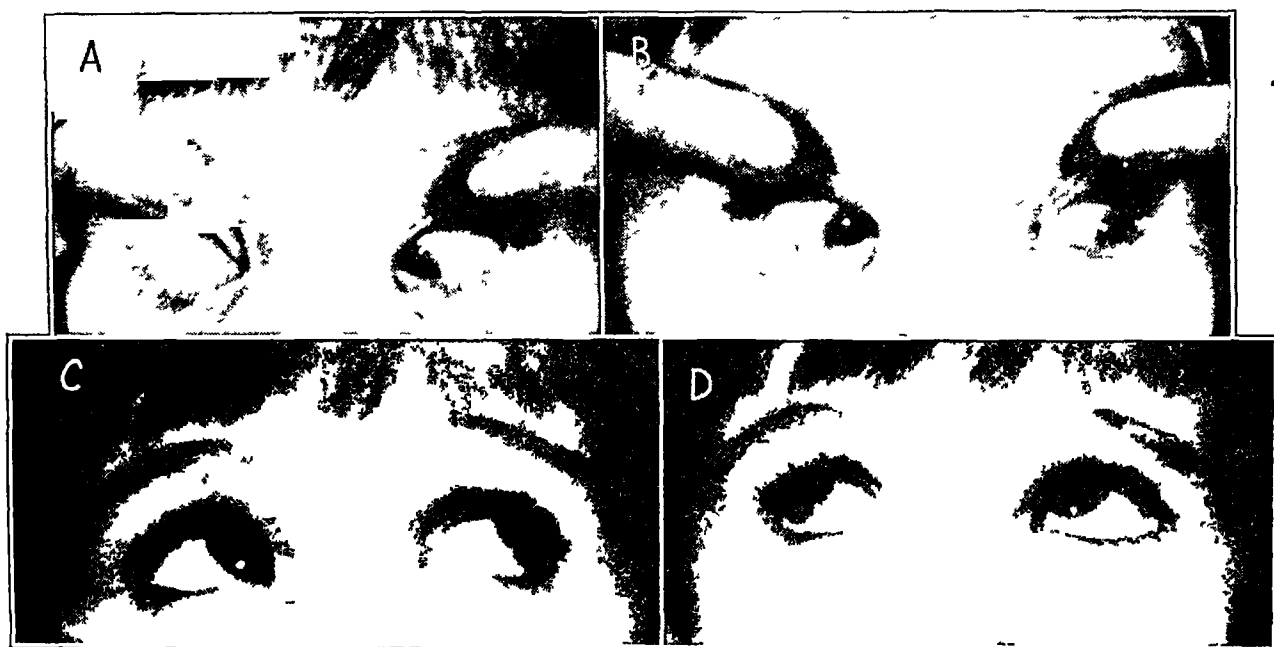


Fig 6—*A*, patient looking down and to the right. The left eye fails to move down completely. *B*, patient looking down and to the left. The eyes move equally well. *C*, patient looking up and to the left. The eyes move equally well. *D*, patient looking up and to the right. The right eye fails to move up completely.

basis of the following reasoning. The right inferior rectus muscle was paretic, so that its normal tone was absent. The right superior rectus muscle, therefore, needed less than the usual innervation to turn this eye up and to the right. Less than the normal amount of innervation was sent to the corresponding yoke muscle, the left inferior oblique, on turning both eyes up and to the right. This simulated a paralysis of the left inferior oblique. Head tilt was not present, and no upward movement of the right eye occurred when the head was tilted on the right shoulder.

*CASE 3—Diagnosis: Primary, congenital paralysis of left superior oblique and inhibitional palsy of right superior rectus.*

E. H., a girl aged 4, had been treated in the orthopedic department for torticollis from the age of 6 months. Surgical treatment was considered, but the idea was abandoned in favor of massage and diathermy. The mother brought the child

to the ophthalmic department on May 24, 1945 because she noted a peculiarity in the position of the eyes

Examination showed that the head was habitually tilted to the right shoulder 15 degrees (measurement of the orthopedic department) The left eye was higher than the right, and the greatest vertical deviation of the eyes occurred when she looked down and to the right There was no vertical difference between the eyes when the child looked down and to the left

When the patient fixed with the left eye, the right eye lagged behind on looking up and to the right, owing to inhibitional palsy of the right superior rectus muscle When the head was forcibly tilted to the left shoulder, the left eye could be seen to make an upward movement

Visual acuity was 6/9 in each eye without correction The patient habitually fixed with the left eye The findings on the synoptophore were as follows Objec-



Fig 7—Head forcibly tilted on the left shoulder The left eye moves up

tive measurement of the deviation in the primary position was 4 degrees of left hypertropia Superposition and fusion were present at the objective angle Diplopia occurred when the hypertropia was not corrected on the instrument, and there was no trace of suppression

All these findings fit in well with the diagnosis of congenital paralysis of the left superior oblique muscle

#### SUMMARY

In cases of primary or congenital paralysis of a vertically acting muscle a differential diagnosis between paralysis of the superior oblique of one side and the superior rectus of the opposite side may be made on the basis of the following signs

- 1 The head is tilted This is the most characteristic sign of paralysis of the superior oblique muscle It is due to the fact that con-

traction of this muscle in the primary position results in 56 per cent of the movement being intorsion. Paralysis of the muscle results, therefore, in extorsion, which can be compensated only by tilting the head in a position which brings the two vertical meridians into parallelism again, i. e., tilting the head on the opposite shoulder. Tilting the head occurs with paralysis of the superior rectus, but is slight, since the superior rectus in the primary position produces only 25 per cent of its pull as intorsion.

2 The head is always tilted toward the side opposite the paralyzed eye. Hence, in a given case of right hypertropia due to paralysis of either the right superior oblique or the left superior rectus muscle, the head will be strongly tilted toward the left shoulder if the right superior oblique is paralyzed and slightly tilted toward the right shoulder if the left superior rectus is at fault.

3 If the head is tilted by the examiner on the shoulder of the same side as the paralyzed eye, this eye will make an upward movement if the superior oblique is paralyzed. If the superior rectus is paralyzed, the eye either will not move at all or will move slightly downward. The physiologic basis for this is given.

Most primary or congenital vertical motor paralyses are due to paralysis of the superior oblique muscle. Those secondary vertical motor paralyses which are associated with a convergent squint and in which the vertical component is seen only in the adducted eye are not due to paralysis of the superior oblique, but may be due to paralysis of the superior rectus—at least they behave more like paralysis of this muscle.

A factor which may confuse the picture in primary or secondary paralysis of a vertically acting muscle is the occurrence of inhibitional palsy of the contralateral antagonist. When this is present, primary paralysis of the superior oblique may easily be mistaken for paralysis of the superior rectus. A physiologic explanation of the phenomenon is given, and illustrative cases are reported.

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## PRODUCTION OF CATARACTS IN CHICKS WITH DINITROPHENOL

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THE OCCURRENCE of cataract following the ingestion of dinitrophenol was first reported in 1935<sup>1</sup> Within the next six years 177 cases had been published in the literature<sup>2</sup>

Thorough experimentation on laboratory animals prior to the release of dinitrophenol for medical use was carried out by Tainter and his fellow workers at Stanford University School of Medicine Further careful work was done following the report of cataracts due to dinitrophenol in man In no instance was it possible to produce cataracts in the ordinary laboratory animals,<sup>3</sup> nor was it possible to produce experimental cataracts by feeding dinitrophenol to animals deficient in vitamins A, B or C<sup>4</sup> The incidence of cataracts could not be increased when dinitrophenol was administered in conjunction with such cataract-producing agents as lactose and galactose<sup>5</sup> The animals used in all instances were mammals

Until recently it was assumed that cataracts did not develop in these laboratory animals because of some difference in their metabolism and that of the human species In 1944 Robbins<sup>6</sup> reported the development of cataracts in young chicks and ducks, and the present preliminary report confirms Robbins' work

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This study was supported by a grant from Mrs Francis I Proctor

From the Division of Ophthalmology, Stanford University School of Medicine

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2 Horner, W D A Study of Dinitrophenol and Its Relation to Cataract Formation, Tr Am Ophth Soc **77** 405, 1941

3 (a) Tainter, M L Growth, Life Span and Food Intake of White Rats Fed Dinitrophenol Throughout Life, J Pharmacol & Exper Therap **63** 51, 1938 (b) Horner, W D Dinitrophenol and Its Relation to Formation of Cataract, Arch Ophth **27** 1097 (June) 1942

4 Tainter, M L, and Borley, W E Influence of Vitamins and Dinitrophenol on the Production of Experimental Cataract, Arch Ophth **20** 30 (July) 1935

5 Borley, W E, and Tainter, M L Influence of Dinitrophenol on the Production of Experimental Cataracts by Lactose, Am J Ophth **21** 1091, 1938

6 Robbins, B H Dinitrophenol Cataract Production in an Experimental Animal, J Pharmacol & Exper Therap **80** 264 (March) 1944

Four  $3\frac{1}{2}$  week old white leghorn pullets were placed on a diet containing 0.25 per cent 2,4 dinitrophenol. Microscopic examination with the slit lamp had previously revealed that the lenses of each chick were entirely clear. Within seven hours after the chicks had been placed on the diet containing dinitrophenol definite lenticular opacities were noted in each eye of all the chicks. The opacities were limited to the anterior and posterior subcapsular regions. The posterior subcapsular area was more densely opaque than the anterior, and in each instance the opacity was denser in the axial portion of the anterior and posterior subcapsular layers and tended to clear toward the periphery. The nucleus and the remainder of the lens cortices remained entirely clear, nor were any other abnormalities noted on microscopic examination with the slit lamp.

Twenty-six hours after the chicks had been placed on the dinitrophenol diet, and approximately seventeen hours after the cataracts described were observed, examination with the slit lamp revealed a marked decrease in the opacification of the lens in spite of continued administration of dinitrophenol in the same concentration. In 2 of the chicks the anterior subcapsular opacities had cleared entirely, and the posterior subcapsular opacities had decreased but were still definitely present. Again, the remaining opacity was denser near the axial portion. In the other chicks the clearing was less dramatic, but definite.

Three and one-half days after the dinitrophenol diet was started, 3 of the chicks had died. Examination of the remaining chick with the slit lamp picture showed that the picture was unchanged. A very fine anterior subcapsular opacity and a somewhat denser posterior subcapsular opacity remained. The remainder of the lenses was clear at all times. The death of these chicks was almost certainly due to the concentrated dose of dinitrophenol, since Tainter<sup>3a</sup> has shown this action of the drug in shortening the life span of white rats. The administration of dinitrophenol was discontinued at this point.

My observations on the experimental cataract in chicks produced by dinitrophenol differed from those of Robbins<sup>6</sup> in that the opacities in the posterior subcapsular area also regressed, although to a somewhat lesser degree than those in the anterior. Robbins reported that the posterior opacities persisted or increased, but his description did not include the findings with slit lamp microscopy. It is of interest to note that the refractile play of colors, the "cloth of gold" appearance, so frequently seen in human cataracts after the ingestion of dinitrophenol was not observed.

This rapid appearance and subsequent regression of cataracts have not been observed in animals other than fowl. Six white mice were placed on a diet containing 0.25 per cent 2,4 dinitrophenol and examined microscopically with the slit lamp at the same time intervals as the



chicks, and no changes in the lens were noted. Six congenitally obese yellow mice<sup>7</sup> were also placed on the same diet and examined at the same time intervals, and no lenticular changes were found. The congenitally obese yellow mice were selected because they show some predisposition to the formation of cataract after ingestion of dinitrophenol<sup>8</sup>.

The interesting observation of Robbins, substantially confirmed here, poses a number of questions. Are the rapidly forming and somewhat transient lenticular opacities which are observed in fowl, and in no other animals, connected in some manner with the increased metabolism and higher temperature of avians? Why do the opacities clear while the dinitrophenol is still being administered? These and other interesting questions will be investigated.

#### SUMMARY

In spite of numerous cataracts observed after the ingestion of dinitrophenol in human subjects, it had not been possible to produce cataract in mammals by the use of this drug, although Robbins accomplished this in young chicks and ducks.

Additional observations on the formation of cataracts in chicks on a diet of dinitrophenol are reported here. The cataracts were limited to the anterior and posterior subcapsular regions and were more marked in the latter. The cataracts were well formed seven hours after the start of the dinitrophenol diet and regressed to a great degree while the drug was still being administered. In white and in congenitally obese yellow mice cataracts failed to develop under the same conditions.

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<sup>7</sup> Danforth, C. H. Hereditary Adiposity in Mice, *J. Hered.* **18** 153, 1927.  
Rytand, D. A. Hereditary Obesity of Yellow Mice, *Proc. Soc. Exper. Biol. & Med.* **54** 340, 1943.

<sup>8</sup> Bettman, J. W. Experimental Dinitrophenol Cataract, *Am. J. Ophth.*, to be published.

# USE OF NEUTRALIZING ANTIBODY TEST IN DIAGNOSIS OF HUMAN TOXOPLASMIC CHOROIDITIS

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With the Assistance of

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THE publication by Sabin<sup>1</sup> of the neutralizing antibody test for the diagnosis of toxoplasmosis encouraged us to utilize this laboratory method in cases of suspected toxoplasmic choroiditis. It was our early ambition to make clinical observations in a few cases, in which laboratory tests had proved that the lesions of choroiditis were undoubtedly positive or negative for *Toxoplasma*, and with this experience to be able to make a presumptive diagnosis of the disease, without necessity of finding a coexisting cerebral calcification or a positive reaction to the neutralizing antibody test to confirm the diagnosis. Such observations during the past three years prompt us to state that until a more accurate or a more convenient means is devised, the neutralizing antibody test must be used if a relatively certain diagnosis is to be made.

Callahan's<sup>2</sup> estimate that the incidence of toxoplasmosis in the St. Louis population is about 2 per cent emphasizes to ophthalmologists the importance of this infectious granuloma, whose only observable manifestation may be a destructive central choroiditis.

## METHODS AND MATERIAL

The neutralizing antibody test for *Toxoplasma* was performed (after Sabin) as follows:

*The Organism*—Both the Sabin<sup>3</sup> R H strain, isolated from the brain tissue of a 6 year old boy who died of encephalitis, and the strain of Wolf, Cowen and

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1 Sabin, A B. *Toxoplasma Neutralizing Antibodies in Human Beings and Morbid Conditions Associated with It*, Proc Soc Exper Biol & Med **51** 6-10 (Oct) 1942.

2 Callahan, W P, Jr. *The Incidence of Toxoplasmic Infection in the St. Louis Area*, in Annual Report of the John and Mary R Markle Foundation, New York, 1944, p 29.

3 Sabin, A B. *Toxoplasmic Encephalitis in Children*, J A M A **116**. 801-807 (March 1) 1941.

Paige,<sup>4</sup> isolated from the spinal cord of an infant who died of encephalomyelitis at 31 days of age, were used in this laboratory. The organism remains viable only by culture in living tissue, murine passage proves the most expedient. The mice are inoculated intracerebrally with 0.03 cc of a 1:10 suspension of infected tissue, and they die at intervals of four to eight days. The virulence of the organism is enhanced by decreasing the intervals between passage. The brains are removed with sterile technic, and sufficient Tyrode's solution is added to make a 1:5 dilution by weight. From this tissue suspension a smear is made, stained and examined for the presence of toxoplasmas. To check for contamination, one tube of aerobic and one tube of anaerobic medium are inoculated and incubated for twenty-four hours. In the refrigerator the uncontaminated *Toxoplasma* suspension will thus be kept viable for ten days, but we have found that to maintain virulence it is advisable to reinoculate within two days.

*The Neutralizing Antibody Test*—Five to 10 cc of blood is taken by venipuncture from the patient for use within twenty-four hours. If tests are not made immediately, the labile antibody of the serum is protected by lyophilization or by freezing at  $-77^{\circ}\text{C}$ . (A known positive serum allowed to stand at room temperature for three hours before centrifugation gave a negative test.) Serums are used undiluted. After the brains are found to be uncontaminated, they are ground with sterile sea sand abrasive, and four times the amount by weight of Tyrode's solution is added and allowed to settle spontaneously for thirty minutes. The supernate, considered to be a 1:5 suspension, is removed into another sterile tube, and subsequent dilutions of 1:10, 1:50, 1:500 and 1:5,000 are made from it. Suitable aliquots of these dilutions are added to equal amounts of Tyrode's solution to make the control mixtures. Similar aliquots are also added to equal amounts of each serum to be tested. The mixtures are shaken gently and allowed to stand thirty minutes, and 0.2 cc is injected intracutaneously with a tuberculin syringe in areas marked on the back of a shaved, clear-skinned rabbit. An appropriate chart is made of the sites of inoculation, and daily checks are made for color and size of the lesion, for size of the necrotic portion and, as the lesions progress, for presence or absence of hemorrhage.

The lesions on the rabbit are papulonecrotic, reaching a maximum about the seventh day after the inoculation and blanching thereafter until the rabbit dies, usually within ten or twelve days. Death is preceded by high fever and increasing weakness.

*Evaluation of Results*—The papular lesions are measured in millimeters for the largest diameter and the widest possible measurement at right angles to it. The diameters of necrosis within the papule are measured in the same way. The area of each lesion is then calculated, using the formula for an ellipse, unless the lesion is circular. By comparative use of the planimeter on tracings of the same lesions, we found estimated measurements of area to be generally within 15 per cent of the actual. Calculations of area for the smallest lesions, which were 2 to 3 mm at their widest diameter, were in error 18 to 33 per cent. For a patient's serum to be considered positive, the area of the serum lesions must be one-half or less that of the corresponding control lesions.

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4 Wolf, A., Cowen, D., and Paige, B. H. Human Toxoplasmosis. Occurrence in Infants as an Encephalomyelitis, Verification by Transmission to Animals, *Science* 89:226-227 (March 10) 1939.

## OBSERVATIONS

The patients under consideration were, for the most part, a selected group, with central chorioretinitis, active or inactive, and a clear vitreous

TABLE 1—*Statistical Summary of Reactions of Serums Tested for Toxoplasma Neutralizing Antibodies*

|   | Number Tested | Reactions |          |          |       |
|---|---------------|-----------|----------|----------|-------|
|   |               | Number    |          | Per Cent |       |
|   |               | Positive  | Negative | Plus     | Minus |
| Patients with chorioretinitis without cerebral calcification  | 28            | 16        | 12       | 57       | 43    |
| Patients with chorioretinitis and with cerebral calcification | 4             | 4         | 0        | 100      | 0     |
| Patients without chorioretinitis                              | 2             | 2         | 0        | 100      | 0     |
| Mothers of toxoplasmic patients                               | 10            | 8         | 2        | 80       | 20    |

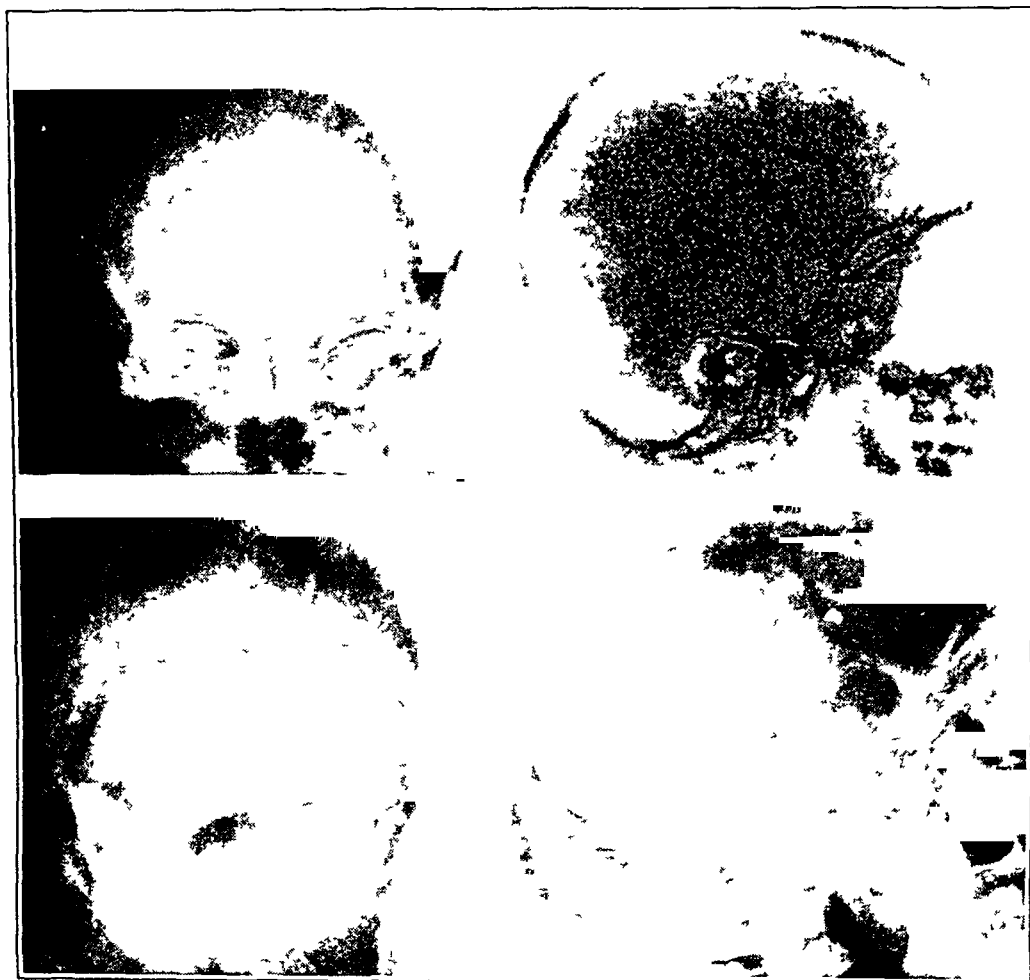


Fig 1—Roentgenograms (anteroposterior and lateral) showing cerebral calcification in 2 patients who had neutralizing antibodies for Toxoplasma in the serum

Among the serums of 32 patients having such chorioretinitis, 20 had neutralizing antibodies (table 1). Four of the 20 had cerebral calcification in addition (fig 1). It is to be emphasized that we have not

seen cerebral calcification with chorioretinitis in persons whose age at onset could be proved to be over 15 years

A survey of cases of probable congenital toxoplasmosis from the literature and from this laboratory (table 2) showed that of 45 patients with choroiditis and a positive reaction to the *Toxoplasma* neutralizing

TABLE 2—Summary of Cases of Toxoplasmic Chorioretinitis, First Observed in Childhood, and Probably a Congenital Infection

| Author  | Patient | Age at Examination | Reaction to Neutralization Test | Cerebral Calcification |
|---|---------|--------------------|---------------------------------|------------------------|
| Wolf, A, and Cowen, D Bull Neurol Inst New York 6 306-371 (July) 1937   | J S     | 2 days             | *                               | +                      |
| Wolf, A, Cowen, D, and Paige, B H Am J Path 15 657-694 (Nov.) 1939  | C D     | 3 days             | *                               | +                      |
| Paige, B H, Cowen, D, and Wolf, A Am J Dis Child 63 474-514 (March) 1942  | L M     | Birth              | *                               | +                      |
| Levin, P M, and Moore, H J Pediat 21 673-679 (Nov) 1942   | G F H   | 3½ mo              | †                               | +                      |
| Sabin, A B Toxoplasmosis, a Recently Recognized Disease of Human Beings, in De Sanctis, A G Advances in Pediatrics, New York, Interscience Publishers, Inc., 1942 | R B     | 6 mo (?)           | +                               | +                      |
| Crothers, B Arch Neurol & Psychiat 49 315-319 (Feb) 1943  | 1       | 12 yr              | +                               | +                      |
|   | 4       | †                  | +                               | +                      |
|   | 5       | †                  | +                               | +                      |
|   | 6       | †                  | +                               | +                      |
|   | 7       | †                  | +                               | +                      |
|   | 9       | 10 yr 7 mo         | +                               | +                      |
|   | 9       | 4 yr 9 mo          | +                               | +                      |
| Koch, F L P, Wolf, A, Cowen, D, and Paige, B H Arch Ophth 29 125 (Jan) 1943   | P D     | 1 wk (?)           | +                               | +                      |
|   | J F     | Birth              | +                               | +                      |
|   | A I     | 4 days             | +                               | +                      |
|   | M B     | 2 mo               | +                               | +                      |
|   | D H     | 4 yr (?)           | +                               | +                      |
|   | C J     | 3 mo               | +                               | —                      |
| Vail D Strong, J C, Jr, and Stephenson, W V Am J Ophth 26 133-140 (Feb) 1943  | N H     | 7 yr               | +                               | —                      |
|   | J S     | 12 yr              | +                               | —                      |
|   | C S     | 7 yr               | +                               | +                      |
|   | O O     | 7 yr               | +                               | +                      |
|   | F W     | Birth (?)          | +                               | —                      |
| Steiner, C, and Kaump, D H J Neuro path & Exper Neurol 3 36-48 (Jan) 1944   | †       | 1 day              | *                               | +                      |
| Wagener, H P Am J M Sc 208 255-264 (Aug) 1944   | †       | Infant             | +                               | +                      |
| Zuelzer, W W Arch Path 38 119 (July) 1944   | H       | 1 mo               | *                               | +                      |
| Heath P, and Zuelzer W W Arch Ophth 33 184-191 (June) 1945  | L H     | 2 mo               | +                               | +                      |
| Heidelman, J H Arch Ophth 34 28-39 (July) 1945  | R S     | 6 mo               | +                               | +                      |
|   | R B     | 7 yr               | +                               | +                      |
|   | N T     | 11 mo              | +                               | +                      |
|   | L H     | 1 mo               | +                               | +                      |
|   | B J     | 9 mo               | +                               | +                      |
|   | L H     | 7 yr               | +                               | †                      |
|   | J O     | 13 yr              | +                               | —                      |
|   | S J     | 8 yr               | +                               | —                      |
|   | T W     | 16 yr              | +                               | —                      |
|   | L S     | 22 yr              | +                               | —                      |
|   | A S     | 15 yr              | +                               | —                      |
| Authors' cases  | M G     | 3 yr               | +                               | +                      |
|   | S H     | 3½ yr              | +                               | +                      |
|   | Mrs S   | 5 yr               | +                               | +                      |
|   | J W     | 3 yr               | +                               | +                      |

\* Toxoplasmas found in the tissue

† Positive reaction to complement fixation test for *Toxoplasma*

‡ Age not mentioned

antibody test, only 7 did not also have cerebral calcification. When the age at onset was over 15 years (table 3), there was no instance of cerebral calcification. The mother of Crother's sixth patient and our own Mrs. G. were the only mothers of a child with toxoplasmosis who had cerebral calcification in addition to neutralizing antibodies in the serum (table 4). Twenty-two other mothers who presumably transmitted the infection in utero had only positive reactions to the neutralizing antibody test, with no other symptoms. Sabin,<sup>1</sup> in a summary, noted that of 15 children with toxoplasmosis, 13 had mothers with neutralizing antibodies in the serum, 1 other child gave positive reaction to a complement fixation test for toxoplasmosis as did his

TABLE 3—*Summary of Cases of Toxoplasmic Choroiditis, First Observed After Childhood and Probably an Acquired Infection*

| Author   | Patient    | Age at Examination, Yr | Reaction to Neutralization Test | Cerebral Calcification |
|--|------------|------------------------|---------------------------------|------------------------|
| Vail, D., Strong, J. C., Jr., and Stephenson, W. V. <i>Am J Ophth</i> 26: 133-140 (Feb) 1943 | H. G.      | 23                     | +                               | —                      |
|  | W. W.      | 29                     | +                               | —                      |
|  | E. C.      | 17                     | +                               | —                      |
| Authors' cases   | Mrs. Q. S. | 23                     | +                               | —                      |
|  | Mrs. H.    | 26                     | +                               | —                      |
|  | M. D.      | 15                     | +                               | —                      |
|  | E. G.      | 36                     | +                               | —                      |
|  | M. P.      | 33                     | +                               | —                      |
|  | G. H.      | 26                     | +                               | —                      |
|  | G. E.      | 35                     | +                               | —                      |
|  | I. K.      | 25                     | +                               | —                      |
|  | K. P.      | 36                     | +                               | —                      |
|  | G. H.      | 36                     | +                               | —                      |
|  | J. P.      | 19                     | +                               | —                      |
|  | E. B.      | 15                     | +                               | —                      |
|  | C. R.      | 50                     | +                               | —                      |
|  | E. D.      | 16                     | +                               | —                      |
|  | J. L.      | 29                     | +                               | —                      |

mother. Of 13 paternal serums described in the literature (including 4 not indicated in table 4), only 1, reported by Sabin, gave a positive reaction. Sixteen of 24 sibsgerman also gave positive reactions to the test. Thus in the families of 45 patients with toxoplasmosis, 56 other members showed positive antibody titers for *Toxoplasma*, only 15 gave negative reactions.

Little is known concerning congenital toxoplasmosis contracted from an infected mother.

Mrs. G., aged 41, and her 10 children presented an unusual opportunity to study the familial incidence of neutralizing antibodies. First born was M. G., two months prematurely, the child had bilateral choroiditis, nystagmus, mental retardation and cerebral calcification, probably present from birth. Mrs. G., M. G. and the next 5 children in the family all had strongly positive reactions to the neutralizing antibody test for toxoplasmosis, the youngest 4 children gave negative, positive, negative and positive reactions, in that order. The mother

TABLE 4.—*Familial Relationships in Cases of Toxoplasmosis*

|  | Author   | Patient  |                         |                              |  | Mother                       |  |                              |  | Father                       |  |                              |  | Sib 1                        |  |                              |  | Sib 2                        |  |                              |  | Sib 3                        |  |                              |  | Sib 4                        |  |   |  | Sib 5 |  |  |  |
|--|--|--|-------------------------|------------------------------|--|------------------------------|--|------------------------------|--|------------------------------|--|------------------------------|--|------------------------------|--|------------------------------|--|------------------------------|--|------------------------------|--|------------------------------|--|------------------------------|--|------------------------------|--|---|--|-------|--|--|--|
|  |  | Initial  | Chorio<br>refi<br>mitis | Neu<br>traliz<br>ing<br>Test | Cerebral<br>Oal<br>traliz<br>ing<br>Test | Neu<br>traliz<br>ing<br>Test | Cerebral<br>Oal<br>traliz<br>ing<br>Test | Neu<br>traliz<br>ing<br>Test | Cerebral<br>Oal<br>traliz<br>ing<br>Test | Neu<br>traliz<br>ing<br>Test | Cerebral<br>Oal<br>traliz<br>ing<br>Test | Neu<br>traliz<br>ing<br>Test | Cerebral<br>Oal<br>traliz<br>ing<br>Test | Neu<br>traliz<br>ing<br>Test | Cerebral<br>Oal<br>traliz<br>ing<br>Test | Neu<br>traliz<br>ing<br>Test | Cerebral<br>Oal<br>traliz<br>ing<br>Test | Neu<br>traliz<br>ing<br>Test | Cerebral<br>Oal<br>traliz<br>ing<br>Test | Neu<br>traliz<br>ing<br>Test | Cerebral<br>Oal<br>traliz<br>ing<br>Test | Neu<br>traliz<br>ing<br>Test | Cerebral<br>Oal<br>traliz<br>ing<br>Test | Neu<br>traliz<br>ing<br>Test | Cerebral<br>Oal<br>traliz<br>ing<br>Test | Neu<br>traliz<br>ing<br>Test | Cerebral<br>Oal<br>traliz<br>ing<br>Test |   |  |       |  |  |  |
|  | Paige, B H, Cowen, D, and Wolf, A<br>63 474 511 (March) 1942   | L M<br>B R   | +                       | +                            | +  | +                            | +  | +                            | +  | +                            | +  | +                            | +  | +                            | +  | +                            | +  | +                            | +  | +                            | +  | +                            | +  | +                            | +  | +                            | +  | + |  |       |  |  |  |
|  | Levin, P M, and Moore, H J<br>Pediat 21 673 679 (Nov)<br>1912  | G F H  | +                       | +                            | +  | +                            | +  | +                            | +  | +                            | +  | +                            | +  | +                            | +  | +                            | +  | +                            | +  | +                            | +  | +                            | +  | +                            | +  | +                            | +  | + |  |       |  |  |  |
|  | Crothers, B Arch Neurol & Psychiat<br>49 315 319 (Feb)<br>1943   | 1<br>2<br>4<br>6<br>8  | +                       | +                            | +  | +                            | +  | +                            | +  | +                            | +  | +                            | +  | +                            | +  | +                            | +  | +                            | +  | +                            | +  | +                            | +  | +                            | +  | +                            | +  | + |  |       |  |  |  |
|  | Koch, F L P, Wolf, A, Cowen, D, and Paige, B II<br>Arch Ophth 29•125 (Jan) 1943                              | P D<br>J F<br>A I<br>M B<br>D H  | +                       | +                            | +  | +                            | +  | +                            | +  | +                            | +  | +                            | +  | +                            | +  | +                            | +  | +                            | +  | +                            | +  | +                            | +  | +                            | +  | +                            | +  | + |  |       |  |  |  |
|  | Vail, D, Strong, J O, Jr, and Stephenson, W V Am J<br>Ophth 26 133 140 (Feb) 1943                            | N H<br>J S<br>O S<br>O C   | +                       | +                            | +  | +                            | +  | +                            | +  | +                            | +  | +                            | +  | +                            | +  | +                            | +  | +                            | +  | +                            | +  | +                            | +  | +                            | +  | +                            | +  | + |  |       |  |  |  |
|  | Zuelzer, W W Arch Path 38 119 (July) 1944 Heath, P,<br>and Zuelzer, W W Arch Ophth 33 161 191 (June)<br>1945 | L H §<br>H S<br>R S<br>R B<br>N T<br>L H<br>B H<br>D M<br>B J<br>S J<br>M G<br>S H | +                       | +                            | +  | +                            | +  | +                            | +  | +                            | +  | +                            | +  | +                            | +  | +                            | +  | +                            | +  | +                            | +  | +                            | +  | +                            | +  | +                            | +  | + |  |       |  |  |  |
|  | Heidelman, J H Arch Ophth 34 28 39 (July) 1945   |  | +                       | +                            | +  | +                            | +  | +                            | +  | +                            | +  | +                            | +  | +                            | +  | +                            | +  | +                            | +  | +                            | +  | +                            | +  | +                            | +  | +                            | +  | + |  |       |  |  |  |
|  | Authors' cases   |  | +                       | +                            | +  | +                            | +  | +                            | +  | +                            | +  | +                            | +  | +                            | +  | +                            | +  | +                            | +  | +                            | +  | +                            | +  | +                            | +  | +                            | +  | + |  |       |  |  |  |

\* Toxoplasmas were seen in the tissues

† This patient gave a positive reaction to a complement fixation test for toxoplasmosis

‡ These sibs german (cases 5 and 7, respectively) had also chorioretinitis, and the condition was diagnosed as toxoplasmosis

§ Sibs 6, 7, 8 and 9 gave negative positive, negative and positive reactions, respectively

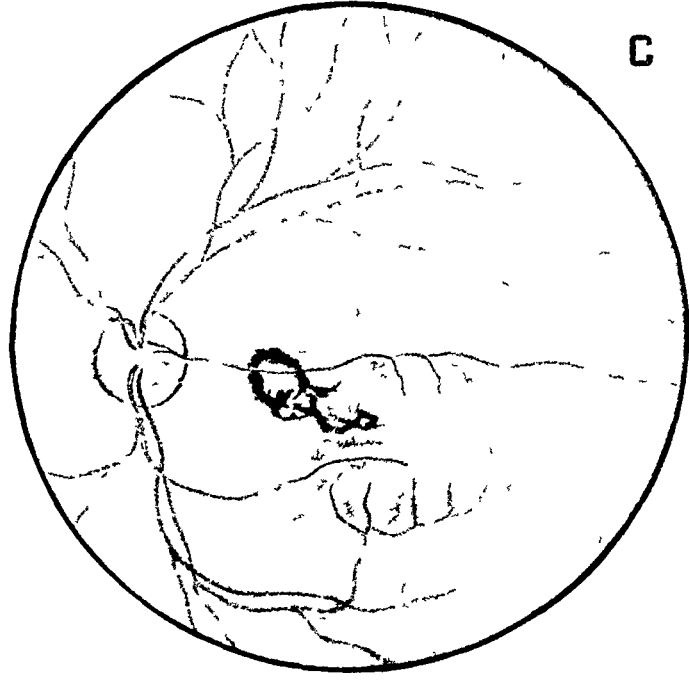
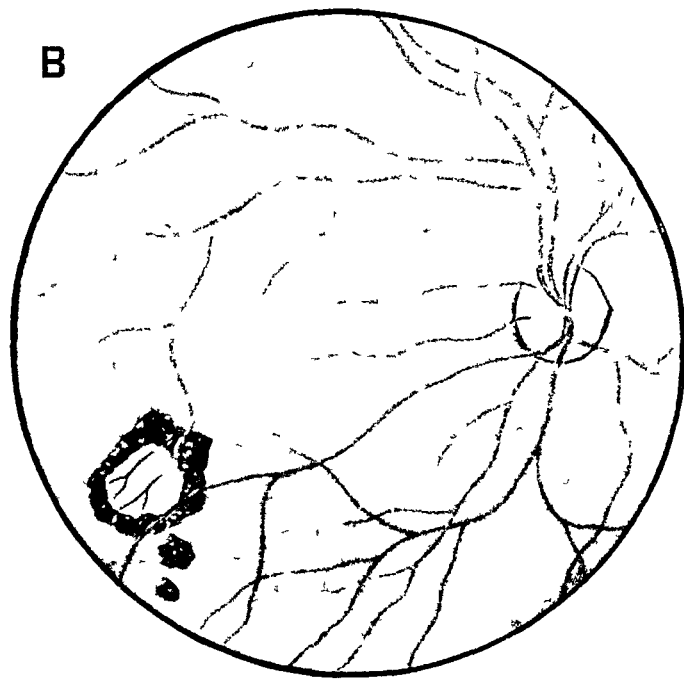
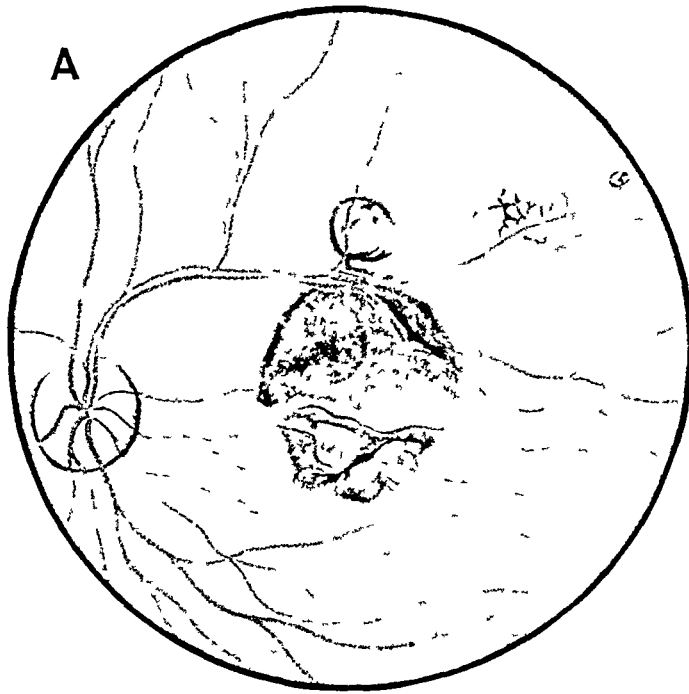


Fig 2—*A* (Mrs S), monocular congenital chorioretinitis after thirty-five years of inactivity *B* (Mrs Q S), healed chorioretinitis of the right eye, which developed during the second pregnancy *C*, acquired central chorioretinitis (left eye of Mrs Q S), showing the deeply pigmented area remaining from activity of the first pregnancy and the much larger, slightly active, lesion which developed during the second pregnancy Fundus drawings by Theodora Bergsland





had typical toxoplasmic calcification of the cerebrum, without chorioretinitis. None of the children except M G had chorioretinitis or gave roentgenographic evidence of calcification of the cerebrum.

Mrs H had neither chorioretinitis nor calcification of the cerebrum but did have a high titer of neutralizing antibodies. First born was S H, who had bilateral choroiditis, mental retardation and calcification of the cerebrum. S H was first examined roentgenographically in 1944, at the age of 3½ years. By comparison, the roentgenograms taken in 1945 showed markedly denser calcification of the original areas with no increase in the number of centers of calcification. The second child was M H, who gave a strongly positive reaction to the neutralizing antibody test but had normal fundi, alert mentality and no cerebral calcification. There were no other children. During the third month of the pregnancy with S H a pet puppy "became blind and had fits and diarrhea," and this may have been the source of the maternal infection.

Mrs S, who gave a positive reaction to the neutralizing antibody test for *Toxoplasma*, had monocular chorioretinitis (fig 2A), probably congenital, which was first observed before the age of 4 years. Roentgenograms also showed calcification of the cerebrum. Her daughter, 3 years old, appeared normal on roentgenographic and fundusoscopic examinations and did not have neutralizing antibodies. In this case it would seem that no infection or immunity was transmitted to the third generation.

Mrs Q S, aged 22, had central choroiditis early in the second month of her first pregnancy and was anxious to receive any benefits from killed typhoid bacilli regardless of possible consequences to the fetus. After a mild febrile reaction to the second injection of typhoid vaccine she miscarried, and the fetus was not saved. The choroiditis slowly subsided. A year later, when she was again gravid, the primary lesion in the left eye again became active, extending within a month to about twice the original size (fig 2B). There also appeared in the right eye a lesion about 2 disk diameters below the macula (fig 2C). This did not progress toward the macula, although no treatment was given. At this time facilities were available for performing the neutralizing antibody test, to which she gave a positive reaction. At term she was delivered of a normal baby, whom we have not yet been able to test for the presence of neutralizing antibodies. Post partum, the choroiditis in the right eye promptly became inactive, and the larger lesion in the left eye gradually subsided. Nine months ago her third pregnancy was accompanied with moderately severe activity in the damaged (left) eye. A thorough course of sulfadiazine was given, without observable effect on the lesion, and her request for a therapeutic abortion was granted as an aid in preserving the central vision in her right eye. No pathologic changes were present in the fetus. After this third pregnancy there was no activity in the lesion in the right eye, and the lesion in the left eye became clinically inactive in the three months after the uterus was emptied. It seems likely that this case is one of the form of toxoplasmosis in which activation of pseudocysts accompanies pregnancy. It may be that Mrs Q S produced sufficient antibodies to protect the fetus from infection but some change associated with pregnancy, possibly chemohormonal, caused a clinically quiescent pseudocyst to become an active chorioretinal lesion. In agreement with the findings of Weinman,<sup>5</sup> our experiments on chronic toxoplasmosis showed that rabbits which have recovered from one

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5 Weinman, D. Chronic Toxoplasmosis, *J Infect Dis* **73** 85-92 (July-Aug) 1943, *Human Toxoplasma*, *Puerto Rico J Pub Health & Trop Med* **20**, 125-161 (Dec) 1944.

inoculation of toxoplasmas carry the organism as pseudocysts in vulnerable tissue for a long time, without symptoms of active infection. Such pseudocysts can then become actively pathogenic by subinoculation of the infected tissue into mice.

Two of 4 laboratory workers who gave negative reactions to the test when they started working with the organism have since given positive responses. Neither of them showed calcification or other clinical evidence of toxoplasmosis. One of them has had a baby which is normal in all respects. A serum from a patient with sympathetic ophthalmia and a serum sent by Dr Theodore Terry, of Boston, from a patient with retinitis exudativa (Coat's disease) showed no neutralizing antibodies for Toxoplasma.

#### SUMMARY

The procedure for the neutralizing antibody test for Toxoplasma and a method for its evaluation are described.

Thirty-two selected patients with chorioretinitis were tested, 20 of these gave positive reactions to the neutralizing antibody test.

Cerebral calcification in patients who had toxoplasmosis with chorioretinitis was not observed when the age at onset was known to be over 15 years. If the disease was present at birth, calcification was evident.

A mother with reactivated toxoplasmic choroiditis and a woman who was probably congenitally infected each gave birth to a normal child. Two children probably infected congenitally with toxoplasmosis had younger siblings-german with antibody protection but no demonstrable infection.

A case of chronic toxoplasmosis is described in which a quiescent chorioretinal lesion became activated during each of three pregnancies.

Major A. B. Sabin, formerly of the Children's Hospital of Cincinnati, and Dr. A. Wolf, of Columbia University College of Physicians and Surgeons, provided the strains of Toxoplasma used.

# EFFECT OF QUALITY OF ILLUMINATION ON THE RESULTS OF THE ISHIHARA TEST

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AND

M CATHERINE RITTLER, A B  
NEW YORK

THIS is the third in a series of reports dealing with the Ishihara test for color blindness. In the first of these reports<sup>1</sup> the fifth edition of the test was evaluated as a means of detecting and analyzing defective color vision. The data reported were collected during the course of a study of 106 persons having defective color vision of varying types and amounts, including 74 who had definite defects in color vision and 32 who had low, but normal, color vision. To study these persons a comprehensive battery of color tests<sup>2</sup> was used, some of which are well known in the field of color blindness testing and some less well known, some have been devised in this laboratory. The fifth edition of the Ishihara test, one of the best known of the shorter editions, was selected for inclusion in the battery of tests. The results obtained from the entire battery aided in the classification of the defect in color vision as to type and extent and at the same time permitted us to evaluate each test of the battery both as a diagnostic or screening medium (the purpose of which is to screen out the subjects with defective color vision from those with normal color vision) and as a medium for classification (the purpose of which is to determine the type and extent of the defect).

Concerning the fifth edition of the Ishihara test, it was concluded that when properly administered the test affords a good rough device for screening persons with defective red-green vision from persons with normal color vision if a performance score of 60 is taken as the critical score, that is, if 60 per cent of the plates are read correctly. In the group tested, no subject with defective color vision scored more than 58 and no subject with normal color vision scored less than 75.

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From the Knapp Memorial Laboratories, Institute of Ophthalmology, Columbia University College of Physicians and Surgeons

1 Hardy, L. H., Rand, G., and Rittler, M. C. Tests for the Detection and Analysis of Color-Blindness. I. An Evaluation of the Ishihara Test, *Arch. Ophth.* 34: 295-302 (Oct.) 1945

2 Hardy, Rand and Rittler,<sup>1</sup> p. 297

The Ishihara test is, however, only a gross test for defective red-green vision. It fails to classify the type of defective color vision (protanopia, protanomaly, deuteranopia, deuteranomaly, tritanopia, tritanomaly<sup>3</sup>) and cannot be used to give a satisfactory evaluation of the extent of the defect, no matter how carefully administered.

In the second of these reports<sup>4</sup> a comparative evaluation was made of three representative editions of the Ishihara test (the fifth,<sup>5</sup> the seventh<sup>6</sup> and the British reprint of the ninth<sup>7</sup>) and of the Ishihara plates included in the American Optical Company's compilation of pseudoisochromatic plates<sup>8</sup>. Twenty-two subjects to whom the entire battery of tests had been administered were available for that work. The general conclusion drawn was that on the whole the three editions of the Ishihara test yield the same type of results in spite of the changes that have been made in the number of plates and in the plates themselves, some of which are improved in one edition as compared with the others while other plates are less effective. The seventh and ninth editions have been improved over the fifth edition so far as detection of protanomalous and protanopic subjects is concerned, but the plates used for the classification of type of red-green defective vision are less successful for deuteranomalous and protanomalous subjects, particularly as reproduced in the seventh edition. None of the editions yields a differential score as to the extent of defective color vision. It seems probable from the data that the critical performance score of 60, marking the dividing line between low normal and defective color vision, holds for the seventh and ninth editions of the test. This critical score, it will be remembered, was established for the fifth edition on the larger group of subjects, which included both observers with defective color vision and those with low normal color vision. The Ishihara plates appearing in the American Optical Company's test

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3 For a simple explanation of these terms, see Hardy, Rand and Rittler,<sup>1</sup> page 298, footnote 14. Additional references are Hardy, L. H., and Rand, G. Recent Developments in Color Vision Testing, Graduate Course, American Academy of Ophthalmology, Outlines of Instructional Courses, Continuous Course nos 6 and 7, 1944. Hardy, L. H., Rand, G., and Rittler, M. C. Color Vision and Recent Developments in Color Vision Testing, Arch Ophth **35** 603-614 (June) 1946. Judd, D. B. Facts of Color-Blindness, J Optic Soc America **33** 294-307 (June) 1943.

4 Hardy, L. H., Rand, G., and Rittler, M. C. Tests for Detection and Analysis of Color Blindness. II. Comparison of Editions of the Ishihara Test, Arch Ophth **35** 109-119 (Feb.) 1946.

5 Ishihara, S. Tests for Colour-Blindness, ed 5, Tokyo, Kanehara, 1925.

6 Ishihara,<sup>5</sup> ed 7, 1936.

7 Ishihara, S. The Series of Plates Designed as Tests for Colour-Blindness, reprinted from ed 9, London, H. K. Lewis & Co., Ltd., 1943.

8 Pseudo-Isochromatic Plates for Testing Color Perception, Philadelphia, American Optical Company, 1940.

were found, however, to be for the most part poor selections and poor reproductions of the original Japanese plates and to have less value for screening deuteranomalous and deuteranopic subjects than the plates as reproduced by Ishihara

The present report describes the effect produced on the results of the Ishihara test by changing the quality of the illumination under which the test is administered. A comparison was made between the two most commonly used illuminants—daylight, for which the tests were designed, and tungsten filament light, which is far too frequently used because of carelessness or lack of proper facilities, combined with ignorance of the important effect of quality of illumination on the results of all tests which employ test material seen by reflected light.

The critical importance of quality of illumination for all tests of this type, particularly for the polychromatic and pseudoisochromatic plates which are being used for the detection of defective color vision, was stressed in the first report of this series,<sup>1</sup> also independently by Hardy.<sup>8a</sup> Because of their great convenience and apparent simplicity of administration, plates of this type have been widely employed in military and industrial fields for many years. We expressed the belief that part of the dissatisfaction that has been reported with regard to the findings with these tests has been due to disregard of the critical importance of the illumination under which the tests were administered. As already indicated, tests of this type were designed to be administered under daylight, and instructions to that effect are given. Too often, however, they have been carelessly administered under artificial light, usually tungsten filament light. The composition of this light, as compared with average daylight, is relatively strong in the long wavelength portion of the spectrum and weak in the short wavelength portion. Consequently, when tungsten light is employed instead of daylight, there will be enhancement of red and yellow pigments, dulling of green and blue pigments and a shift in hue of the mixed colors toward the long wavelengths.

To determine the effect of this incorrect administration, subjects with defective color vision were tested with different editions of the Ishihara test, utilizing the same amounts (25 foot candles) of different illuminants. The responses were compared when the illuminant was changed from artificial daylight to tungsten filament light. The daylight illumination was obtained from the nearest practical equivalent to ICI Illuminant C, that provided by a Macbeth daylight lamp (tungsten lamp plus filter of Corning Daylight glass) designed to operate at approximately 6,750°K. The tungsten filament illumination was provided by a 75 watt Mazda gas-filled lamp, operating at rated voltage, at a color temperature of approximately 2,848°K. This illumination is equivalent

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8a Hardy, L. H. Standard Illuminants in Relation to Color-Testing Procedures, *Arch Ophth* 34:278-282 (Oct) 1945

to ICI Illuminant A. For convenience, these illuminations will be called "daylight" and "tungsten" throughout the present report.

The effect of this change in illumination on the results of the test was determined for the fifth, seventh and ninth (British reprint) editions of the Ishihara test and for the Ishihara plates included in the American Optical Company's compilation of pseudoisochromatic plates. Only the plates intended for testing color-blind literates were used, of which there are 12 in the fifth edition, 24 in the seventh and ninth editions and 10 in the American Optical Company's test. These plates consist of six series. Series 1 and 2 are of the "transformation pattern" type, in which the subject with defective color vision sees a different pattern from that which the subject with normal color vision sees, series 3 and 4 are of the "vanishing digit" type, in which the pattern is not seen at all by the subject with defective color vision, series 5 contains a "hidden digit," which is supposedly seen only by a subject with defective color vision, and series 6 is intended for the differential classification of the type of defective red-green vision. A fuller description of the six series of plates is given in the first report of this series.<sup>1</sup> In the fifth edition there are 2 plates of each series, in the seventh and ninth editions, 4 plates of each series, and in the American Optical Company's test, 4 plates of series 1, 4 plates of series 2 and 2 plates of series 5. Differences found in the effect of change of illumination from edition to edition are, of course, due to differences in the pigments used, which in some instances are pronounced.

Twenty-two subjects to whom the entire battery of tests<sup>2</sup> had been administered were available for the present work. They included 12 subjects with anomalous trichromasy, of whom 7 had the deuteranomalous and 5 the protanomalous type, and 10 with dichromasy, of whom 5 were deuteranopic and 5 were protanopic. Differences in the effect of change of illumination found in the subjects with the different types of defective color vision are due both to the extent or degree of the defect and to the characteristic reaction of each type to the color combinations used in the various plates of the Ishihara test.

Throughout the work the testing distance was about 30 inches (76 cm). Care was taken to avoid any specular reflection from the test plates. To this end, the angle of illumination was approximately 45 degrees and the angle of view 90 degrees.

The general conclusion to be drawn from the study is that performance scores on the Ishihara test tend to be higher for persons with defective red-green vision (i.e., a greater number of correct responses are given) when the illuminant is tungsten light than when it is daylight, most significantly in subjects with deuteranomaly and deuteranopia. The effect is so marked that a substantial proportion of deuteranomalous subjects (42 per cent) score within normal limits.

when tungsten light is employed Further, the Ishihara test is a poorer medium for the differential classification of type of red-green defect when the illuminant is tungsten light Fewer subjects are correctly classified by the test, more are not classified at all, and a greater number of protanomalous and protanopic subjects are incorrectly classified when the illumination is shifted from daylight to tungsten

In detail, the results are summarized in tables 1 to 3 They will be discussed under three headings (1) effect of quality of illumination on responses to the individual plates, (2) effect of quality of illumination on performance scores on the entire test and (3) effect of quality of illumination on the differential classification of deuteranopia and protanopia, deuteranomaly and protanomaly In each table the results for daylight illumination are given in roman type, those for tungsten illumination in boldface

#### EFFECT OF QUALITY OF ILLUMINATION ON RESPONSES TO THE INDIVIDUAL PLATES

Table 1 shows for each type of defective color vision and for each illuminant the percentage of subjects who pass the individual plates of each edition, the plates being designated by both series number and plate number as they appear in the edition under consideration The first four horizontal rows of figures in roman type under each edition show these percentages for each type of defective color vision when the test is administered under daylight, the first four rows in boldface under each edition show these percentages when the test is administered under tungsten light These data demonstrate the value of the individual plates for detecting each type of defective color vision when the test is administered under the illuminant indicated The two bottom rows under each edition show the percentages for the subjects with defective color vision as a group and demonstrate the value of the individual plates for the simple detection of defective color vision

The following statements summarize the more important changes produced by administering the tests under tungsten illumination instead of daylight

- 1 In general a higher percentage of subjects having defective color vision pass the individual plates of the Ishihara test when tungsten illumination instead of daylight is used This result is most pronounced for deuteranomalous subjects and is particularly evident with the plates as reproduced in the fifth edition It is next most significant for deuteranopic subjects especially with the Ishihara plates as reproduced in the American Optical Company's selection In other words, fewer subjects with defective red-green vision, particularly the deuteranomalous and deuteranopic types, are detected by the plates of the



TABLE 1—Effect of Illumination on Responses to the Individual Plates of the Ishihara Test for Each Type of Defective Color Vision \*

| Percentage of Subjects with each Type Passing Individual Plates |                    |                         |          |                             |    |          |          |    |          |          |    |          |          |    |          |          |    |          |          |     |    |          |    |    |    |    |
|---|--------------------|-------------------------|----------|-----------------------------|----|----------|----------|----|----------|----------|----|----------|----------|----|----------|----------|----|----------|----------|-----|----|----------|----|----|----|----|
| Type of Defective Color Vision                                  | Number of Subjects | Quality of Illumination | Series 1 |                             |    | Series 2 |          |    | Series 3 |          |    | Series 4 |          |    | Series 5 |          |    | Series 6 |          |     |    |          |    |    |    |    |
|   |                    |                         | Plate No |                             |    | Plate No |          |    | Plate No |          |    | Plate No |          |    | Plate No |          |    | Plate No |          |     |    |          |    |    |    |    |
|   |                    |                         | 2        | 3                           |    | 4        | 5        | 6  | 7        | 8        | 9  | 10       | 11       | 12 | 13       | 14       | 15 | 16       | 17       | 18  | 19 | 20       | 21 | 22 | 23 | 24 |
| Anomalous trichromasy<br>Deuteranomaly                          | 7                  | Daylight                | 57       | 72                          |    | 0        | 0        | 0  | 11       | 11       | 29 |          |          |    |          |          |    |          |          |     |    |          |    |    |    |    |
|   |                    | Tungsten                | 86       | 72                          |    | 57       | 14       | 72 | 86       | 57       | 72 |          |          |    |          |          |    |          |          |     |    |          |    |    |    |    |
|   | 5                  | Daylight                | 80       | 100                         |    | 0        | 0        | 0  | 0        | 0        | 0  |          |          |    |          |          |    |          |          |     |    |          |    |    |    |    |
|   |                    | Tungsten                | 80       | 60                          |    | 0        | 0        | 20 | 20       | 20       | 40 |          |          |    |          |          |    |          |          |     |    |          |    |    |    |    |
| Dichromasy<br>Deutanopia  | 5                  | Daylight                | 0        | 0                           |    | 0        | 0        | 0  | 0        | 0        | 0  |          |          |    |          |          |    |          |          |     |    |          |    |    |    |    |
|   |                    | Tungsten                | 0        | 0                           |    | 0        | 0        | 20 | 20       | 0        | 20 |          |          |    |          |          |    |          |          |     |    |          |    |    |    |    |
|   | 5                  | Daylight                | 60       | 60                          |    | 0        | 0        | 0  | 0        | 0        | 0  |          |          |    |          |          |    |          |          |     |    |          |    |    |    |    |
|   |                    | Tungsten                | 60       | 20                          |    | 0        | 0        | 0  | 0        | 0        | 0  |          |          |    |          |          |    |          |          |     |    |          |    |    |    |    |
| All types of defective color vision                             | 22                 | Daylight                | 50       | 50                          |    | 0        | 0        | 0  | 5        | 5        | 9  |          |          |    |          |          |    |          |          |     |    |          |    |    |    |    |
|   |                    | Tungsten                | 59       | 41                          |    | 18       | 5        | 32 | 36       | 23       | 36 |          |          |    |          |          |    |          |          |     |    |          |    |    |    |    |
|   |                    |                         |          | Seventh Edition (24 Plates) |    |          |          |    |          |          |    |          |          |    |          |          |    |          |          |     |    |          |    |    |    |    |
|   |                    |                         |          | Plate No                    |    |          | Plate No |    |          | Plate No |    |          | Plate No |    |          | Plate No |    |          | Plate No |     |    | Plate No |    |    |    |    |
| Anomalous trichromasy<br>Deuteranomaly                          | 7                  | Daylight                | 43       | 14                          | 0  | 14       | 0        | 0  | 0        | 14       | 14 | 0        | 0        | 29 | 29       | 0        | 0  | 43       | 29       | 14  | 0  | 43       | 57 | 43 |    |    |
|   |                    | Tungsten                | 72       | 29                          | 0  | 29       | 0        | 57 | 43       | 29       | 57 | 0        | 57       | 57 | 43       | 43       | 14 | 57       | 57       | 57  | 57 | 29       | 57 | 86 | 57 |    |
|   | 5                  | Daylight                | 0        | 20                          | 0  | 0        | 0        | 0  | 0        | 0        | 0  | 0        | 0        | 0  | 20       | 0        | 0  | 0        | 0        | 0   | 0  | 0        | 10 | 60 | 40 | 20 |
|   |                    | Tungsten                | 0        | 20                          | 0  | 0        | 0        | 0  | 0        | 0        | 0  | 0        | 0        | 0  | 0        | 0        | 0  | 0        | 0        | 0   | 0  | 0        | 20 | 40 | 80 | 20 |
| Dichromasy<br>Deutanopia  | 5                  | Daylight                | 0        | 0                           | 20 | 0        | 0        | 0  | 0        | 0        | 0  | 0        | 0        | 20 | 0        | 0        | 0  | 20       | 0        | 0   | 0  | 0        | 0  | 0  | 0  | 0  |
|   |                    | Tungsten                | 0        | 0                           | 0  | 60       | 20       | 20 | 0        | 0        | 0  | 0        | 0        | 40 | 20       | 60       | 40 | 80       | 100      | 100 | 80 | 0        | 0  | 0  | 0  | 0  |
|   | 5                  | Daylight                | 0        | 20                          | 0  | 0        | 0        | 0  | 0        | 0        | 0  | 0        | 0        | 0  | 20       | 0        | 0  | 0        | 20       | 20  | 20 | 0        | 0  | 0  | 0  | 0  |
|   |                    | Tungsten                | 0        | 0                           | 0  | 0        | 0        | 0  | 0        | 0        | 0  | 0        | 0        | 0  | 0        | 0        | 0  | 0        | 20       | 20  | 20 | 40       | 0  | 40 | 0  | 20 |
| All types of defective color vision                             | 22                 | Daylight                | 14       | 14                          | 5  | 5        | 0        | 0  | 0        | 5        | 5  | 0        | 0        | 14 | 18       | 0        | 18 | 14       | 9        | 5   | 23 | 32       | 23 | 18 |    |    |
|   |                    | Tungsten                | 23       | 11                          | 0  | 9        | 36       | 5  | 23       | 14       | 9  | 18       | 0        | 18 | 27       | 18       | 27 | 14       | 41       | 45  | 45 | 14       | 36 | 45 | 27 |    |

Ninth Edition, British Reprint (24 Plates)

|                                     |             | Plate No |    |    |    | Plate No |    |     |    | Plate No |    |    |    | Plate No |    |    |    | Plate No |    |    |    | Plate No |    |    |    |
|-------------------------------------|-------------|----------|----|----|----|----------|----|-----|----|----------|----|----|----|----------|----|----|----|----------|----|----|----|----------|----|----|----|
|                                     |             | 2        | 3  | 4  | 5  | 6        | 7  | 8   | 9  | 10       | 11 | 12 | 13 | 14       | 15 | 16 | 17 | 18       | 19 | 20 | 21 | 22       | 23 | 24 | 25 |
| Anomalous trichromasy               | Deutanomaly | 43       | 43 | 0  | 14 | 72       | 14 | 57  | 0  | 14       | 29 | 0  | 14 | 14       | 0  | 0  | 0  | 14       | 14 | 0  | 14 | 0        | 57 | 29 | 14 |
|                                     |             | 29       | 43 | 14 | 29 | 100      | 57 | 100 | 0  | 43       | 14 | 0  | 14 | 14       | 14 | 0  | 0  | 29       | 43 | 14 | 43 | 14       | 72 | 29 | 0  |
|                                     | Protanomaly | 20       | 20 | 0  | 0  | 0        | 0  | 0   | 0  | 0        | 0  | 0  | 0  | 0        | 0  | 0  | 0  | 0        | 0  | 0  | 0  | 20       | 60 | 20 | 20 |
|                                     |             | 0        | 20 | 20 | 0  | 60       | 0  | 40  | 0  | 0        | 0  | 0  | 0  | 0        | 0  | 0  | 0  | 0        | 0  | 0  | 0  | 20       | 60 | 40 | 20 |
| Dichromasy                          | Deutanopia  | 0        | 0  | 0  | 0  | 20       | 0  | 20  | 0  | 0        | 0  | 0  | 0  | 0        | 0  | 0  | 0  | 0        | 0  | 0  | 0  | 0        | 0  | 0  | 0  |
|                                     |             | 20       | 20 | 0  | 0  | 100      | 60 | 100 | 20 | 0        | 0  | 0  | 0  | 0        | 0  | 0  | 0  | 80       | 80 | 80 | 80 | 0        | 0  | 0  | 0  |
|                                     | Protanopia  | 0        | 20 | 0  | 0  | 0        | 0  | 0   | 0  | 0        | 0  | 0  | 0  | 0        | 0  | 0  | 0  | 0        | 20 | 20 | 40 | 0        | 20 | 0  | 0  |
|                                     |             | 20       | 20 | 0  | 0  | 20       | 0  | 0   | 0  | 0        | 0  | 0  | 0  | 0        | 0  | 0  | 0  | 20       | 20 | 20 | 40 | 20       | 0  | 20 | 0  |
| All types of defective color vision | Daylight    | 18       | 23 | 0  | 5  | 27       | 5  | 23  | 0  | 5        | 9  | 0  | 5  | 5        | 0  | 0  | 0  | 9        | 9  | 5  | 14 | 5        | 36 | 14 | 9  |
|                                     | Tungsten    | 18       | 27 | 9  | 9  | 73       | 32 | 64  | 5  | 14       | 5  | 0  | 5  | 5        | 5  | 0  | 0  | 32       | 36 | 27 | 41 | 14       | 36 | 23 | 5  |

Ishihara Plates, American Optical Company's Test (10 Plates)

|                                     |               | Plate No |    |    |    | Plate No |     |     |     | Plate No |  |  |  | Plate No |  |    |    | Plate No |  |
|-------------------------------------|---------------|----------|----|----|----|----------|-----|-----|-----|----------|--|--|--|----------|--|----|----|----------|--|
|                                     |               | 5        | 6  | 11 | 12 | 19       | 20  | 41  | 42  |          |  |  |  |          |  | 33 | 34 |          |  |
| Anomalous trichromasy               | Deuteranomaly | 86       | 43 | 0  | 43 | 72       | 0   | 72  | 57  |          |  |  |  |          |  | 57 | 57 |          |  |
|                                     |               | 100      | 72 | 29 | 72 | 86       | 86  | 100 | 100 |          |  |  |  |          |  | 29 | 43 |          |  |
| Protanomaly                         | Daylight      | 10       | 0  | 0  | 0  | 0        | 0   | 0   | 0   |          |  |  |  |          |  | 20 | 20 |          |  |
|                                     | Tungsten      | 60       | 0  | 0  | 20 | 20       | 0   | 40  | 40  |          |  |  |  |          |  | 20 | 40 |          |  |
| Dichromasy                          | Deuteranopia  | Daylight | 20 | 20 | 0  | 20       | 0   | 0   | 40  | 40       |  |  |  |          |  | 20 | 20 |          |  |
|                                     |               | Tungsten | 60 | 40 | 0  | 40       | 100 | 100 | 100 | 100      |  |  |  |          |  | 60 | 60 |          |  |
| Protanopia                          | Daylight      | 40       | 0  | 0  | 0  | 0        | 0   | 0   | 0   |          |  |  |  |          |  | 0  | 0  |          |  |
|                                     | Tungsten      | 40       | 0  | 0  | 0  | 0        | 0   | 0   | 60  | 40       |  |  |  |          |  | 20 | 20 |          |  |
| All types of defective color vision | Daylight      | 50       | 18 | 0  | 18 | 23       | 0   | 32  | 27  |          |  |  |  |          |  | 27 | 27 |          |  |
|                                     | Tungsten      | 68       | 32 | 9  | 36 | 55       | 50  | 77  | 73  |          |  |  |  |          |  | 32 | 41 |          |  |

\* Percentage of subjects with each type of defective color vision passing each plate of the Ishihara test, editions 5, 6 and 9 (British reprint) and the Ishihara plates in the American Optical Company's test when the test was administered under daylight and under tungsten light. Each plate is designated by series number and by plate number as it appears in the edition under consideration.

Ishihara test when it is incorrectly administered under tungsten illumination

2 Without our entering into a detailed analysis of the changes produced in the appearance of each plate as the result of the change in illuminant from daylight to tungsten light the following comments are probably justified with regard to the factors which produce a higher percentage of normal responses among subjects with defective red-green vision when the test is administered under tungsten illumination

*Series 1 and 2 (transformation pattern)*—In the plates of series 1 one or two digits, composed in general of blue-red and yellow-red disks, are seen by the subject with normal color vision on a background composed of blue-green and yellow-green disks. To the subject with defective red-green vision, to whom the yellow-red portion of the digit and the yellow-green background have little if any differentiation, only the blue-red and blue-green disks stand out from the background, forming for him a bluish pattern on a yellowish background. The pattern is thus transformed for the subject with defective color vision into a different one from that seen by the subject with normal color vision, e.g., from an 8 to a 3. In the plates of series 2 approximately the same combination of colors is used but with background and pattern reversed, that is, blue-green and yellow-green disks form the digits on a background of blue-red and yellow-red disks. Again, the pattern seen by the subject with defective red-green vision is formed by those disks which have a blue component. Since the effect of tungsten light is to enhance red and yellow pigments, to dull green and blue pigments and to shift the hue of mixed colors toward the longer wavelengths, the digits seen by the subject with normal color vision are emphasized, and those seen by the subject with defective red-green vision are dulled, by the use of this illuminant. The result is that fewer persons with defective red-green vision give the expected response when the illumination is changed from daylight to tungsten light. Instead, they more frequently give the normal response and obtain a passing score, as is shown in table 1, or else they often see no digit at all and fail the test—a change in response which is not shown in table 1 but is revealed by an analysis of individual responses.

The plates of series 2 are most affected by the change in illumination as reproduced in the ninth edition (British reprint) of the Ishihara test and in the American Optical Company's selection of Ishihara plates—some of the plates of series 2 of these editions being passed by all the deuteranomalous and deuteranopic subjects.

*Series 3 and 4 (vanishing digit)*—In the plates of these series the contrast between digit and background is obviously intensified under tungsten light as compared with daylight. The result is that fewer

subjects with defective color vision fail to read the digit, thus, more succeed in passing the plates

*Series 5* (hidden digit) —In the plates of this series the digit, which is supposedly seen only by subjects with defective color vision, is bluish. Under tungsten illumination this coloration is less pronounced than under daylight. The result is that fewer persons with defective color vision see this bluish "hidden digit," and thus, again, more of them give the normal response (no digit seen) and pass the plates. It may be mentioned that this hidden digit is seen under daylight illumination by many having normal color vision, who by this reaction fail to pass the plate. It is rarely visible to the subject with normal color vision, however, when viewed by him under tungsten light.

In all editions of the Ishihara test studied the responses given by the deuteranomalous and deuteranopic subjects to the plates of this series are significantly affected by the change in illumination. Most deuteranopic subjects, and with some plates all the deuteranopic subjects, failed to see the pattern under tungsten illumination, thus passing the particular plate. The responses given by the protanomalous subjects and by the majority of the protanopic subjects, however, were not affected by the change of illumination. That is, they saw the hidden digit under both daylight and tungsten light, thus failing to pass the plate. The reason for this may perhaps be found in the tendency of protanomalous and protanopic subjects to see the hidden digit, which is bluish, as lighter than the background, which is in general composed of red, orange and yellow disks. These background colors, it will be remembered, appear darker to protanomalous and protanopic subjects than they do to deuteranomalous, deuteranopic and normal persons.

*Series 6* (diagnostic plates) —These plates carry two digits (e.g., 26), one in red and one in red-purple disks, on a background of gray disks of different brightnesses. Protanopic subjects, who have a neutral band in the red of the normal color system, just too purplish to be a spectral red, are supposed to see only the red-purple digit (the 6), and deuteranopic subjects, who have a neutral band in the red-purple zone of the normal color system, well outside the limits of the visible spectrum, are supposed to see only the red digit (the 2). The effect of the incorrect use of tungsten illumination on the plates of this series is to intensify the red component of both digits and to dull the blue component of the red-purple digit. The result is that more subjects with defective color vision see both digits correctly against their gray background, and thus more succeed in passing at least some of the plates of this series. This result occurred among deuteranomalous, protanomalous and protanopic subjects. It did not occur with any of our deuteranopic subjects.

The effect of the change in quality of the illumination from daylight to tungsten light on the diagnostic possibilities of the plates of series 6 is discussed in a later section

#### EFFECT OF QUALITY OF ILLUMINATION ON PERFORMANCE SCORES ON THE ENTIRE TEST

Table 2 shows the performance scores obtained on the entire test for each of the editions of the Ishihara test under consideration and for the 10 Ishihara plates in the American Optical Company's test when administered under daylight and under tungsten light. In this table are given for each type of defect in color vision (*a*) the average score achieved by the group, (*b*) the median, or middle, score for each group and (*c*) the range of scores from lowest to highest achieved by the subjects within each group. A score of 100 indicates that correct responses were given to all the plates of the test, a score of 0, that no correct responses were given, and scores between 0 and 100 indicate the percentage of plates to which correct responses were given. As in table 1, the first four rows of figures in roman type under each edition give the data for each type of defective color vision when the test is administered under daylight, the first four rows in boldface under each edition give the data when the test is administered under tungsten light. These data thus demonstrate the effect of changing the quality of illumination from daylight to tungsten light on the scores achieved on the entire test for the subjects with each of the types of defective color vision. The two bottom rows of figures under each edition show this effect for the subjects with defective color vision as a group and demonstrate the significance of performance scores on the entire test for the simple detection of the presence of defective color vision when the test is administered under the two types of illumination.

The findings presented in table 2 may be summarized as follows

- 1 With the single exception of the protanomalous subjects tested with the seventh edition of the Ishihara test, the average performance scores are always higher when the test is administered under tungsten light than when it is administered under daylight. The improvement in score is greatest for deuteranomalous subjects, particularly with the fifth edition of the test, and for deuteranopic subjects, particularly with the Ishihara plates used by the American Optical Company. The change in average score with protanomalous and protanopic subjects is of little consequence for all editions, except perhaps the American Optical Company's Ishihara plates.

- 2 With the exception of the protanomalous subjects when tested with the seventh edition and of the protanopic subjects when tested with the ninth edition, the median performance scores also are higher when

the test is administered under tungsten light. Again, the increase in score is highest with deuteranomalous and deuteranopic subjects.

3 In conformity with the higher performance scores attained by most subjects with defective red-green vision under tungsten light,

TABLE 2—*Effect of Quality of Illumination on Performance Scores on the Ishihara Test for Each Type of Color Defective Vision \**

| Type of<br>Defective Color<br>Vision             | Number<br>of<br>Subjects | Quality of<br>Illumina-<br>tion | Scores  |        |          |
|--|--------------------------|---------------------------------|---------|--------|----------|
|  |                          |                                 | Average | Median | Range of |
| Fifth Edition                                    |                          |                                 |         |        |          |
| Anomalous trichromasy                            |                          |                                 |         |        |          |
| Deuteranomaly                                    | 7                        | Daylight                        | 20      | 17     | 0 53     |
|  |                          | Tungsten                        | 59      | 58     | 25 92    |
| Protanomaly                                      | 5                        | Daylight                        | 18      | 17     | 8 33     |
|  |                          | Tungsten                        | 28      | 33     | 8 42     |
| Dichromasy                                       |                          |                                 |         |        |          |
| Deuteranopia                                     | 5                        | Daylight                        | 0       | 0      | 0        |
|  |                          | Tungsten                        | 15      | 8      | 8 25     |
| Protanopia                                       | 5                        | Daylight                        | 13      | 17     | 8 17     |
|  |                          | Tungsten                        | 15      | 17     | 0 25     |
| All types of defective color vision              | 22                       | Daylight                        | 14      | 17     | 0 53     |
|  |                          | Tungsten                        | 32      | 25     | 0 92     |
| Seventh Edition                                  |                          |                                 |         |        |          |
| Anomalous trichromasy                            |                          |                                 |         |        |          |
| Deuteranomaly                                    | 7                        | Daylight                        | 18      | 17     | 0 33     |
|  |                          | Tungsten                        | 44      | 42     | 21 67    |
| Protanomaly                                      | 5                        | Daylight                        | 8       | 12     | 0 17     |
|  |                          | Tungsten                        | 7       | 4      | 4 17     |
| Dichromasy                                       |                          |                                 |         |        |          |
| Deuteranopia                                     | 5                        | Daylight                        | 2       | 4      | 0 4      |
|  |                          | Tungsten                        | 26      | 25     | 13 37    |
| Protanopia                                       | 5                        | Daylight                        | 4       | 0      | 0 17     |
|  |                          | Tungsten                        | 7       | 4      | 4 17     |
| All types of defective color vision              | 22                       | Daylight                        | 9       | 6      | 0 33     |
|  |                          | Tungsten                        | 23      | 19     | 4 67     |
| Ninth Edition (British Reprint)                  |                          |                                 |         |        |          |
| Anomalous trichromasy                            |                          |                                 |         |        |          |
| Deuteranomaly                                    | 7                        | Daylight                        | 19      | 21     | 0 42     |
|  |                          | Tungsten                        | 30      | 25     | 21 54    |
| Protanomaly                                      | 5                        | Daylight                        | 6       | 4      | 0 12     |
|  |                          | Tungsten                        | 11      | 12     | 0 21     |
| Dichromasy                                       |                          |                                 |         |        |          |
| Deuteranopia                                     | 5                        | Daylight                        | 2       | 0      | 0 8      |
|  |                          | Tungsten                        | 27      | 29     | 21 29    |
| Protanopia                                       | 5                        | Daylight                        | 5       | 4      | 0 17     |
|  |                          | Tungsten                        | 9       | 4      | 4 17     |
| All types of defective color vision              | 22                       | Daylight                        | 9       | 4      | 0 42     |
|  |                          | Tungsten                        | 20      | 21     | 0 54     |
| Ishihara Plates, American Optical Company's Test |                          |                                 |         |        |          |
| Anomalous trichromasy                            |                          |                                 |         |        |          |
| Deuteranomaly                                    | 7                        | Daylight                        | 50      | 50     | 20-70    |
|  |                          | Tungsten                        | 71      | 80     | 50 100   |
| Protanomaly                                      | 5                        | Daylight                        | 8       | 0      | 0 30     |
|  |                          | Tungsten                        | 24      | 20     | 10 40    |
| Dichromasy                                       |                          |                                 |         |        |          |
| Deuteranopia                                     | 5                        | Daylight                        | 18      | 10     | 0 50     |
|  |                          | Tungsten                        | 66      | 60     | 40 90    |
| Protanopia                                       | 5                        | Daylight                        | 4       | 0      | 0 10     |
|  |                          | Tungsten                        | 18      | 20     | 0 30     |
| All types of defective color vision              | 22                       | Daylight                        | 23      | 10     | 0 70     |
|  |                          | Tungsten                        | 47      | 45     | 0 100    |

\* Performance score is percentage of the plates to which correct responses were given.

the range of scores from lowest to highest is in general shifted upward and in many instances is widened when this illuminant is used. This effect is shown in the last column of table 2. As is seen in this column, the upper value of this range for deuteranomalous subjects tested with the fifth edition of the Ishihara test is shifted above the critical score of 60, the score that was established in an earlier report<sup>1</sup> as the dividing line between normal performance and the performance of subjects with defective color vision when the test is properly administered under daylight.

An analysis of individual cases in this group of deuteranomalous subjects reveals that of the 7 tested, 3, or 42 per cent, would not have been screened from the normal if the test had been administered under tungsten illuminant. The scores for these 3 subjects jumped, respectively, from 17 to 92, from 58 to 83 and from 25 to 75 when the illumination was shifted from daylight to tungsten light. In other words, the criterion of 60 per cent for the performance on the fifth edition of the Ishihara test cannot be used when tungsten light is employed.

In order to show that the Ishihara test is not unique among pseudo-isochromatic tests in being influenced by the quality of illumination under which the test is administered, the following brief statement of results obtained with the complete American Optical Company test<sup>8</sup> may be given. As was the case with the Ishihara test, only the plates designed for literate subjects were used. For the same 22 subjects with defective color vision whose comparative scores on the Ishihara test are given in this report, the average scores and ranges of scores for the entire test of the American Optical Company obtained when the illuminant was changed from daylight to tungsten light are summarized.

*Deuteranomaly*—The average score increased from 37 to 52, the range of scores changed from 28 to 55 to 30 to 70,

*Protanomaly*—The average score increased from 28 to 33, the range of scores changed from 20 to 35 to 25 to 43,

*Deuteranopia*—The average score increased from 17 to 35, the range of scores changed from 15 to 23 to 25 to 48,

*Protanopia*—The average score increased from 16 to 18, the range of scores changed from 5 to 20 to 13 to 25.

The improvement in performance scores on the American Optical Company test when the illuminant was shifted from daylight to tungsten almost precisely parallels that noted on the Ishihara test, that is, the improvement was most marked for deuteranomalous and deuteranopic subjects.

EFFECT OF QUALITY OF ILLUMINATION ON THE DIFFERENTIAL  
CLASSIFICATION OF DEUTERANOPIA AND PROTANOPIA,  
DEUTERANOMALY AND PROTANOMALY

As was stated previously, the plates of series 6 of the Ishihara test were designed as a means of classifying the type of defect among subjects with defective red-green vision. On each plate of this series there are two digits, the left one composed of red disks of less brightness than the background (gray) disks, and the right one composed of red-purple disks of approximately the same brightness as the background disks. According to Ishihara, the subject with the deuteranopic type of defective red-green vision misses the red-purple digit and is able to read only the lighter red digit, since this type has a neutral band in the red-purple of the normal color system and has luminosity values that approximate those of normal subjects. The subject with the protanopic type of defective red-green vision, on the other hand, misses the lighter red digit and is able to read only the red-purple digit, since this type has a neutral band nearer the red of the spectrum and perceives red as darker in brightness than do normal and deuteranopic subjects. The effectiveness of these plates for the classification of the type of defect in red-green vision, as reproduced in the fifth, seventh and ninth editions of the test, was analyzed in previous reports<sup>9</sup> when the test was administered under daylight, as directed by Ishihara. Table 3 gives the results for these editions of the test when the illumination was changed from daylight to tungsten light. This change in illumination causes a noticeable shift in the hue of the red-purple digit toward red and a shift in the hue of the red digit toward yellow-red.

In scoring the responses to these plates, we used the criterion previously discussed<sup>1</sup>. That is, a defect in red-green vision was called "classified" when one digit was read correctly and the other was not seen at all or was read incorrectly. When both digits were read correctly, when neither was read correctly or when one was read incorrectly and the other was not seen at all, the defect was called "not classified". In short, a "hit and miss" response is necessary in order to utilize any plate of series 6 as a test for classification of type of defect in red-green vision. It seems reasonable to require a "hit and miss" response on at least 50 per cent of the plates used for this purpose.

Table 3 indicates the results obtained.

1 The percentage of deuteranomalous subjects correctly classified was decreased by the use of tungsten illumination. For the fifth edition the decrease was from 86 to 57 per cent, for the seventh edition, from 57 to 43 per cent. For the ninth edition there was no change. Since with this type of subjects with defective red-green vision no incorrect

<sup>9</sup> Hardy, Rand and Rittler (footnotes 1 and 4)



classifications were made, the percentages for which no classification could be made were proportionately increased. This result was due to the ability of more of the deuteranomalous subjects to read both the red and the red-purple digit under tungsten illuminant, when only the red digit was seen under daylight. Apparently, the hue of the

TABLE 3—*Effect of Quality of Illumination on the Differential Classification of Deuteranopia and Protanopia, Deuteranomaly and Protanomaly\**

| Type of Defective Color Vision  | Number of Subjects | Quality of Illumination | Percentage Correctly Classified by at Least 50% of the Plates | Percentage Incorrectly Classified by at Least 50% of the Plates | Percentage Not Classified by at Least 50% of the Plates |
|---------------------------------|--------------------|-------------------------|---|---|---|
| Fifth Edition                   |                    |                         |   |   |   |
| Anomalous trichromasy           |                    |                         |   |   |   |
| Deuteranomaly                   | 7                  | Daylight                | 86  | 0   | 14  |
|                                 |                    | Tungsten                | 57  | 0   | 43  |
| Protanomaly                     | 5                  | Daylight                | 80  | 0   | 20  |
|                                 |                    | Tungsten                | 0   | 80  | 20  |
| Dichromasy                      |                    |                         |   |   |   |
| Deuteranopia                    | 5                  | Daylight                | 100   | 0   | 0   |
|                                 |                    | Tungsten                | 100   | 0   | 0   |
| Protanopia                      | 5                  | Daylight                | 60  | 0   | 40  |
|                                 |                    | Tungsten                | 40  | 20  | 40  |
| Seventh Edition                 |                    |                         |   |   |   |
| Anomalous trichromasy           |                    |                         |   |   |   |
| Deuteranomaly                   | 7                  | Daylight                | 57  | 0   | 43  |
|                                 |                    | Tungsten                | 43  | 0   | 57  |
| Protanomaly                     | 5                  | Daylight                | 40  | 20  | 40  |
|                                 |                    | Tungsten                | 0   | 60  | 40  |
| Dichromasy                      |                    |                         |   |   |   |
| Deuteranopia                    | 5                  | Daylight                | 100   | 0   | 0   |
|                                 |                    | Tungsten                | 100   | 0   | 0   |
| Protanopia                      | 5                  | Daylight                | 60  | 0   | 40  |
|                                 |                    | Tungsten                | 0   | 20  | 80  |
| Ninth Edition (British Reprint) |                    |                         |   |   |   |
| Anomalous trichromasy           |                    |                         |   |   |   |
| Deuteranomaly                   | 7                  | Daylight                | 86  | 0   | 14  |
|                                 |                    | Tungsten                | 86  | 0   | 14  |
| Protanomaly                     | 5                  | Daylight                | 60  | 0   | 40  |
|                                 |                    | Tungsten                | 0   | 60  | 40  |
| Dichromasy                      |                    |                         |   |   |   |
| Deuteranopia                    | 5                  | Daylight                | 100   | 0   | 0   |
|                                 |                    | Tungsten                | 100   | 0   | 0   |
| Protanopia                      | 5                  | Daylight                | 60  | 0   | 40  |
|                                 |                    | Tungsten                | 40  | 40  | 20  |

\* Analysis of the value of the plates of series 6 of the fifth, seventh and ninth (British reprint) editions of the Ishihara test as a means of differentiating types of defective red green vision when the test is administered under daylight and under tungsten light.

red-purple digit was shifted by the yellower illumination into a color region to which these subjects were more sensitive.

2 The percentage of deuteranopic subjects correctly classified was not changed by the use of tungsten illumination. All the deuteranopic subjects were correctly classified by at least 50 per cent of the plates of series 6 when both illuminants were used.

3 In the classification of protanomalous and protanopic subjects, the deleterious effect of the yellower illumination was most strikingly demonstrated. The result was a decrease in the percentage of correct classifications and, more significantly, an increase in the occurrence of incorrect classifications. In the latter case, the red digit, which was not seen by some of the protanomalous and protanopic subjects under daylight illumination, was seen under tungsten illumination because under this light its hue was apparently shifted toward the yellow by a sufficient amount to bring it into a color region to which these subjects were more sensitive, whereas the red-purple digit, usually seen by them under daylight illumination, was not seen under tungsten light because its hue was apparently shifted toward red by a sufficient amount to bring it into the color region to which these subjects were less sensitive. Thus, an incorrect classification of deuteranopia, instead of the correct one of protanopia, was more frequently obtained under tungsten light than under daylight. This result was particularly frequent for the protanomalous subjects when tested with all three editions of the Ishihara test.

#### CONCLUSIONS

In spite of the small number of subjects used in this comparative study of the effect of quality of illumination on the results of the Ishihara test taken as typical of polychromatic and pseudoisochromatic tests the following conclusions seem to be justified when the test is incorrectly administered under tungsten light, instead of under daylight, as is directed by the author of the test.

- 1 When tungsten light is used as the illuminant, the performance scores attained by all the deuteranomalous and deuteranopic subjects tested are higher than when daylight is used. The responses of protanopic and protanomalous subjects are little affected by this change in quality of illumination.

- 2 A substantial number of deuteranomalous subjects are sufficiently aided in giving normal responses by the incorrect use of tungsten light to take them out of the class of persons with defective color vision when judged by the performance score; that is, their scores fall within the normal limits established for daylight illumination.

- 3 There is a decrease in the number of subjects who are correctly classified for type of defective red-green vision when tested under tungsten light, as compared with the number so classified when tested under daylight, and an increase in the number of protanomalous and protanopic subjects who are incorrectly classified.

We wish to stress once more the critical importance of strict observance of correct conditions of illumination during the administration of polychromatic tests which employ test material seen by reflected light.

## CYCLOFUSIONAL MOVEMENTS

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IT IS generally recognized that cyclofusional movements of the two eyes can occur in the interest of maintaining single binocular vision, especially in the unnatural and the forced optical conditions that, for example, can be produced in the stereoscope. A historical survey shows that this recognition has come not without controversy. Nagel,<sup>1</sup> it seems, was the first to point out that a cyclofusional movement took place when horizontal lines, observed in the stereoscope, were rotated in opposite directions. Independently, von Helmholtz<sup>2</sup> found the same evidence with an arrangement of prisms when rotating the images in the two eyes in opposite directions. At the same time, Hering,<sup>3</sup> while not denying the possibility of such movements, was unconvinced by the experiments of Nagel and von Helmholtz, but more especially by his own attempts to find such movements with a stereoscope. Only later, after Nagel had repeated both the experiments of von Helmholtz and his own previous work<sup>4</sup> and had verified the results, did Hering find what he considered to be the weakness of his experiments and then accept the evidence for cyclofusional movements.<sup>5</sup>

The classic experiments which demonstrate that cyclofusional movements can be enforced optically are those of Hofmann and Bielschowsky.<sup>6</sup> In these, cards of identical print were used on the

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From the Division of Research in Physiological Optics, Dartmouth Eye Institute, Dartmouth Medical School

1 Nagel, A. *Das Sehen mit zwei Augen*, Leipzig, C F Winter, 1861, p 51

2 von Helmholtz, H. *Ueber die Augenbewegungen*, Heidelberg Jahrb d Literatur, 1865, p 258, Helmholtz's *Treatise on Physiological Optics*, translated and edited by J P C Southall, Rochester, N Y, The Optical Society of America, 1924, vol 3, pp 59-62

3 Hering, E. *Die Lehre vom binocularen Sehen*, Leipzig, Wilhelm Engelmann, 1868, cited in *Wissenschaftliche Abhandlungen*, Leipzig, Georg Thieme, 1931, vol 2, pp 56-62, *Ueber die Rollung des Auges um die Gesichtslinie*, Arch f Ophth **15** (pt 1) 1-16, 1869

4 Nagel, A. *Ueber das Vorkommen von wahren Rollungen des Auges um die Gesichtslinie*, Arch f Ophth **14** (pt 2) 228-246, 1868

5 Hering, E. *Der Raumsinn und die Bewegungen des Auges*, in von Hermann, L. *Handbuch der Physiologie*, Leipzig, F C W Vogel, 1879, vol 3, p 504

6 Hofmann, F B, and Bielschowsky, A. *Der Willkur entzogenen Fusionsbewegungen der Augen*, Arch f d ges Physiol **80** 1-40, 1900, cf pp 20-28

two sides of a haploscope. Above the center of one card and below the center of the other, horizontal lines were drawn. On looking into the haploscope, one sees a single card of print with two horizontal lines that appear parallel. In slowly rotating the cards in opposite directions about their centers, it was found that these lines continued to appear parallel until the cards had been rotated even by as much as 5 to 8 degrees, that then they slowly deviated from parallelism and, finally, that the print was seen double. It is clear that so long as the lines appeared parallel with this rotation the eyes must have been making cyclotorsional movements at the same rate.

In America, Perry,<sup>7</sup> in 1895, and Stevens,<sup>8</sup> in 1897, described methods for measuring cyclofusional amplitudes (the limits of torsion through which the targets can be rotated and the print remain single) when using a stereoscopic device. In 1926 Ames<sup>9</sup> reported experiments also showing the existence of cyclofusional movements with lines and with stereoscopic pictures, and he later suggested that the cyclofusional amplitudes be included in any thorough study of ocular measurements.<sup>10</sup> Verhoeff,<sup>11</sup> however, continued to deny, even until the early 1930's, the possible existence of cyclofusional movements. He accounted for cyclofusional amplitudes entirely on the basis of Panum's fusional areas. That fusional areas do contribute to the cyclofusional amplitudes cannot be doubted,<sup>12</sup> and this was recognized by Hofmann and Bielschowsky. In 1934 Verhoeff repeated Hofmann and Bielschowsky's experiment with improved apparatus and verified their results completely.

Using a telescope to observe distinctive markings on the iris, Brecher,<sup>13</sup> in 1934, reported measuring the actual cyclorotations of

7 Perry, C. H. Rotation in Oblique Astigmatism, *Ophth Rec* 5:175-178, 1895-1896.

8 Stevens, G. T. The Directions of the Apparent Vertical and Horizontal Meridians of the Retina, *Arch Ophth* 26:181-203, 1897.

9 Ames, A., Jr. Cyclophoria, *Am J Physiol Optics* 7:3-38, 1926.

10 Ames, A., Jr., and Gliddon, G. H. Ocular Measurements, *Tr Sect Ophth, A. M. A.*, 1928, pp. 102-175.

11 Verhoeff, F. (a) A Description of the Reflecting Phorometer and a Discussion of the Possibilities Concerning Torsions of the Eyes, *Tr Am Ophth Soc* 8:490-503, 1899, (b) A New Instrument for Measuring Heterophoria and the Combining Power of the Eyes, *Bull Johns Hopkins Hosp* 10:87-92, 1899, (c) A Theory of Binocular Perspective and Some Remarks upon Torsions of the Eyes, *Ann Ophth* 2:201-229, 1902, (d) Cycloduction, *Tr Am Ophth Soc* 32:208-228, 1934.

12 Tschermak, A. Augenbewegungen, in Bethe, A., von Bergmann, G., Emden, G., and Ellinger, A. *Handbuch der normalen und pathologischen Physiologie*, Berlin, Julius Springer, 1930, vol. 12, pt. 2, pp. 1001-1094.

13 Brecher, G. A. Die optokinetische Auslösung von Augenrollung und rotatorischem Nystagmus, *Arch f d ges Physiol* 234:13-28, 1934.

the eyes in haploscopic cycloduction tests. Against this, however, in a brief and incomplete note, Beasley and Peckham,<sup>14</sup> when using a similar technic, reported that no actual torsions could be observed.

No longer is there any question that cyclofusional movements can be enforced. Evidence has also been produced to show that parallel, or conjugate, torsional movements (as against the opposing, or disjunctive, torsional movements involved in cyclofusional amplitudes) can, under appropriate conditions, be induced optically,<sup>15</sup> and even optokinetically.<sup>13</sup> These studies, however, do not include the parallel compensatory torsions that accompany changes in positions of the head and body, movements which are thoroughly covered in the literature in other connections.

All experiments dealing with enforced cyclofusional movements involve the use of similar patterns in a stereoscope or haploscope or of prism and mirror devices, by which the image for one eye can be rotated about its optic axis with respect to the image of the other eye. The essential facts regarding these movements may be briefly summarized as follows. There is a small lag in the cyclotorsions of the eyes behind the actual torsions of the images, and hence these movements are to be considered delayed and relatively slow movements. The amplitude within which the ocular movements can accompany the torsions of the targets varies greatly with the amount of detail in those patterns, being least for a single horizontal line and at a maximum for print or for stereoscopic pictures. A single vertical line has not been considered suitable on account of the influence of stereopsis, which makes it appear inclined toward or away from the observer.

Cyclofusional movements, like the other fusional movements, are subject to training, have residual tendencies after a movement in one direction, show varying reaction times and vary with the individual subject. The two eyes make essentially equal but opposite cyclotorsions, even though only the image of one eye is rotated,<sup>6</sup> a fact indicating that the innervations leading to those movements are supplied equally to the two eyes. Herzau<sup>16</sup> showed, moreover, that the cyclofusional movements as measured by the amplitudes were independent of an enforced vertical divergence of the two eyes and that, therefore, these movements arise in an independent muscular synergy.

One concludes, then, that in addition to the apparent torsional movements that occur according to Listing's law, or those parallel reflex

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14 Beasley, W. C., and Peckham, R. H. An Objective Study of Cyclotorsion, *Psychol. Bull.* **33** 741-742, 1936.

15 Noji, R. Ueber optisch erzwungene parallele Rollungen der Augen, *Arch. f. Ophth.* **122** 562-571, 1929.

16 Herzau, W. Ueber das Verhältnis von erzwungener Vertikaldivergenz und Rollung bei der Fusion, *Arch. f. Ophth.* **122** 59-74, 1929.

cyclotorsional movements that tend to compensate for inclinations of the head and body, or those changes in torsion associated with convergence and elevation and depression of the eyes, the external muscles of the eyes can cooperate in the interest of maintaining binocular single vision to provide cyclotorsions about the visual axes, which may remain fixed. These movements fall into the category of reflex movements, characterized by Hofmann<sup>17</sup> as "psycho-optical" reflexes in that they depend on the attention of the observer and yet when that attention is given they act as reflex movements and can be neither induced nor suppressed spontaneously<sup>18</sup>.

In the present paper, a series of experiments will be described which provide a new contribution to knowledge of the nature of these movements<sup>19</sup>. All the evidence from these experiments shows that cyclofusional movements of the eyes take place in the interest of fusion more freely than has heretofore been realized. These movements are determined in the main by the type and orientation of the configurations in the visual field, especially by the vertical contours of the configuration and, to a small extent, by attention. In complex fields of contours demanding torsions of different amounts, these movements tend to be a compromise of the antagonistic compulsions to fusion.

Suppose, as is illustrated in figure 1, that the two eyes are fixating a line which is perpendicular to the visual plane, and suppose, further, that this line appears precisely vertical to the observer—vertical in the sense that the top does not appear nearer or farther away than the bottom. This means, then, that the images of this line fall on meridians of the retinas of the two eyes which are stereoscopically zero, that is, the horizontal disparity between the images of any point on the line

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17 Hofmann, F. B. *Die Lehre vom Raumsinn*, in Graefe, A., and Saemisch, T. *Handbuch der gesamten Augenheilkunde*, Berlin, Julius Springer, 1925, vol. 3, chap. 13, p. 312.

18 W. Feilchenfeld (*Ueber die Willkürlichkeit der Augenbewegungen insbesondere der Rollung der Augen*, *Klin. Monatsbl. f. Augenh.* **88**: 514-517, 1932) believes the evidence is still inconclusive that torsional movements can never take place voluntarily.

19 The experiments were part of a study of the space eikonometer, in which it was recognized that cyclotorsions of the eyes could interfere with the measurement of meridional aniseikonic errors at oblique axes. The literature referred to in this study is as follows: (a) Ames, A., Jr. *The Space-Eikonometer Test for Aniseikonia*, *Am. J. Ophth.* **28**: 248-262, 1945. (b) Ogle, K. N. *Association Between Aniseikonia and Anomalous Binocular Space Localization*, *Arch. Ophth.* **30**: 54-64 (July) 1943. (c) Ogle, K. N., and Madigan, L. F. *Astigmatism at Oblique Axes and Binocular Stereoscopic Spatial Localization*, *ibid.* **33**: 116-127 (Feb.) 1945. (d) Burian, H. M., and Ogle, K. N. *Meridional Aniseikonia at Oblique Axes*, *ibid.* **33**: 293-309 (April) 1945. (e) Ogle, K. N. *Theory of Space-Eikonometer*, *J. Optic. Soc. America* **36**: 20-32, 1946.

is zero. These meridians in the strictest functional sense are, therefore, said to be corresponding meridians.

Now, if the line is inclined with the top nearer to the observer, the retinal images are no longer vertical, but each is deviated in a rotary sense in an opposite direction about the axis of fixation (see insert, fig 1). The line will appear inclined in space because of the stereoscopic response to the horizontal disparities between the images of the two eyes which exist for all parts of the line except the point of fixation. The total angular deviation between the images in the two eyes will be designated as a declination and indicated by  $\delta$ . The term "declina-

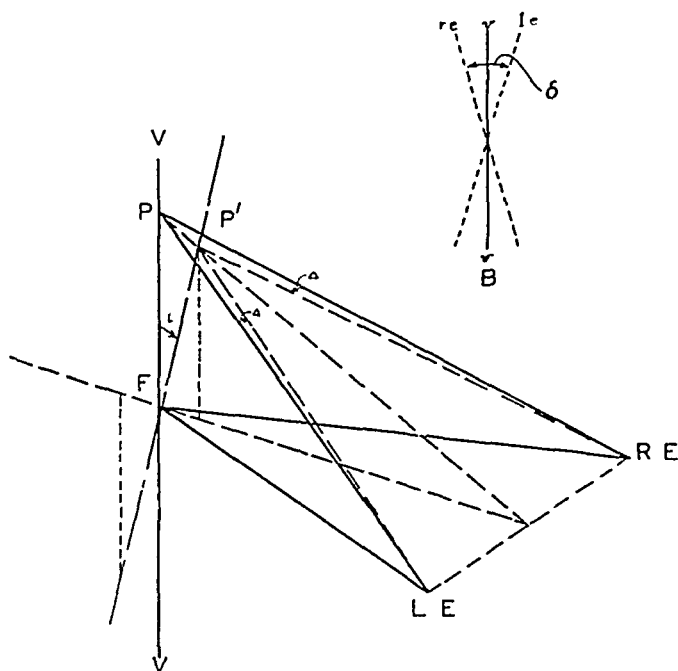


Fig 1—Perspective drawing illustrating the disparities introduced by an inclined line in space and the equivalent rotation of the images of the two eyes.

tion," which was coined by Stevens,<sup>20</sup> is used here to designate the total angular deviation between the images of the two eyes measured from those meridians of the eyes which determine the stereoscope vertical.

The angle of inclination,  $\iota$ , of the line, measured from the vertical, is related to the angle of declination,  $\delta$  by

$$\tan \iota = \frac{b}{2a} \tan \delta \quad (1)$$

where  $b$  is the visual distance and  $2a$  is the interpupillary distance.

20 Stevens, G. T. *A Treatise on the Motor Apparatus of the Eye*, Philadelphia, F. A. Davis Company, 1906.

and where  $b$  is large as compared with  $a^{10c}$  The tabulation which follows shows approximate values of  $\delta$  for various inclinations of the line, computed from this formula for a visual distance of 2 meters and for an interpupillary distance of 64 mm It will be seen that

| $\iota$ | $\delta$ | $\iota$ | $\delta$ | $\iota$ | $\delta$ |
|---------|----------|---------|----------|---------|----------|
| 0°      | 0 00°    | 20°     | 0 60°    | 40°     | 1 40°    |
| 5°      | 0 14°    | 25°     | 0 76°    | 45°     | 1 66°    |
| 10°     | 0 28°    | 30°     | 0 94°    | 50°     | 1 90°    |
| 15°     | 0 44°    | 35°     | 1 14°    | 55°     | 2 36°    |

small angles of declination,  $\delta$ , will be associated with relatively large angles of inclination,  $\iota$  Even an inclination of 10 degrees will be associated with a declination between the retinal images of only 0.3 degrees The apparent magnitude of the inclination for a given declination will, of course, be greater as the visual distances increase

In normal circumstances, and provided the positions of the eyes remain unchanged, the inclination of the line for a given  $\delta$  should be correctly seen in stereoscopic perception If, however, owing to a fusional compulsion from the disparate images of the line, a cyclotorsional movement of  $\tau$ , degrees occurs (in figure 1, an incyclotorsional movement), to bring the images nearer corresponding meridians, the effective declination,  $\delta$ , will be reduced, and even eliminated Then the inclined line would (or would tend to) appear vertical

This is exactly what happens if a long white thread uniformly illuminated is inclined in the median plane and observed through unlike apertures in a dark room where no empiric clues or motives for spatial localization are evident Only as the angle of inclination becomes large will the thread appear inclined, and even then only by a small degree Moreover, if, in addition, a horizontal white thread is stretched in the field of view along the axis of rotation of the inclined thread, the latter does then appear inclined, though perhaps not to the full extent At times, with these two lines, the perception will seem confused and unsteady A cyclofusional movement in this case that would reduce the declination between the images of the inclined line would also introduce a declination between the images of the horizontal line, which, in turn, would exert a compulsion for a torsion in the opposite direction Thus, the addition of the horizontal line dampens or stabilizes the degree to which cyclofusional movements can overcome the declination between the images of the inclined line

Such subjective experiments are unsatisfactory, and it is almost impossible to eliminate the empiric factors of varying brightness and change in angular size, which increase the more the line is inclined Furthermore, one is restricted in the degree of inclination that can be obtained without the subjects seeing the frame which supports the line To overcome these difficulties in the experiments to be described, all configurations used in the field of view were fixed in a vertical



position, and the declinations between the images were introduced optically

The optical device, which will be designated as the geared unit,<sup>19</sup> consists of two matched, meridional size (afocal magnifying) lenses that are mounted in geared rings. The dimensions of the two rings are such that the teeth mesh and the separation of the lenses (which are 44 mm in diameter) will correspond to an average interpupillary distance. When activated by a small pinion alined to one of the rings, the two lenses will then rotate equally but in opposite directions. A suitable drum attached to the shaft of the pinion is calibrated to read directly the change in declination for vertical (and horizontal) lines in tenth of a degree. The drum reads zero when the axes of the lenses are parallel and vertical.

A meridional size lens magnifies the image seen through it in one meridian only and consequently will introduce rotary deviations of the images of all lines in space not parallel with or perpendicular to the

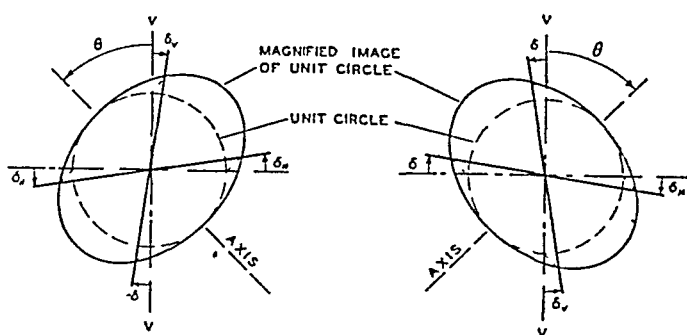


Fig 2—Illustration of how the geared meridional size lenses introduce a rotary deviation between the images of vertical and horizontal lines

meridian of magnification. When the axis of the lens is placed obliquely, the images of vertical and horizontal lines will always be deviated toward the meridian of magnification, almost equally but in directions opposite each other (scissors effect) (fig 2). The magnitude of the declination angle,  $\delta$ , between the images of the vertical lines (and horizontal lines, though the declination will be in an opposite direction) will be related to the angle  $\theta$ , through which the two geared lenses have been rotated, by

$$\tan \delta = 2 \frac{M - 1}{M + 1} \sin 2\theta \quad (2)$$

where  $M$  is the magnification of the lenses.<sup>21</sup> For most of the experiments 2 per cent meridional size lenses were used. For small angles

<sup>21</sup> Ogle, K. N. Meridional Magnifying Lens Systems in the Measurement and Correction of Aniseikonia, *J Optic Soc America* **34** 302-312, 1944

of rotation,  $\delta$  is approximately 0.034 degree per degree  $\Theta$ , with a maximum  $\delta$  (when  $\Theta = \pm 45^\circ$ ) of about 1.1 degree. If the lenses are rotated so that the axes converge above the unit, the declination of the images of the vertical lines ( $\delta_v$ ) will be taken as positive, if rotated to converge down, it will be taken as negative. No size differences between the images of the two eyes will be introduced by the unit in the vertical or the horizontal meridian. On a special lens-testing instrument<sup>22</sup> these units were calibrated carefully, not only for the distance at which they were to be used before the eyes but also for the particular viewing distance used.

In the series of studies to be described, the nature of the cyclofusional movements in any given experiment will be deduced from the data that depend on the stereoscopic perception of certain test configurations in the field of view as influenced by the introduction of declinations. The investigation is in three parts, dealing with (1) the determination of the stereoscopic thresholds to changes in declination, (2) the determination of the apparent orientation of the test configurations as perceived stereoscopically and (3) the statistical results of a measurement obtained on nearly 400 subjects with a fixed (space eikonometer) test configuration.

For the special studies in the investigation, 3 subjects were used, whose ocular characteristics are summarized in the following tabulation.

| Subject | Uncorrected Visual Acuity | Refractive Error (Subjective Measurement)                            | Heterophoria at 6 Meters | P D * mm |
|---------|---------------------------|--|--------------------------|----------|
| V J E   | R E 20/15<br>L E 20/15    | + 0.12 D cyl, ax 160<br>+ 0.12 D cyl, ax 180                         | 1½Δ exophoria            | 62       |
| N W     | R E 20/15<br>L E 20/15    | + 0.25 D sph<br>+ 0.25 D sph   | ¼Δ exophoria<br>½Δ RH †  | 60       |
| K N O   | R E 20/15+<br>L E 20/15   | + 0.25 D sph — 0.25 D cyl, ax 25<br>+ 0.25 D sph — 0.12 D cyl, ax 10 | ½Δ esophoria<br>¼Δ RH †  | 64       |

\* P D indicates interpupillary distance

† RH indicates right hyperphoria

The greater part of the data were taken by the first and last subjects, who were trained in making stereoscopic observations.

## STEREOSCOPIC THRESHOLDS TO INCLINED SPATIAL CONFIGURATIONS AND RELATION TO CYCLOFUSIONAL MOVEMENTS OF THE EYES

### APPARATUS AND METHOD

In all determinations the head of the observer was held fixed with a suitable head rest and a wax bite (fig. 3), which prevented depth discrimination by the parallax associated with head movements. Directly in front of the observer, at a distance of 3 meters, a rigid wooden square frame (1.5 meters on a side) was set up in the vertical position with its plane at right angles to the median plane of the observer, and was centered with respect to that plane and at the level of the

<sup>22</sup> Ogle, K. N., and Ames, A., Jr. Ophthalmic Lens Testing Instrument, J. Optic Soc. America **33** 137-142, 1943.

eyes of the observer. The various test configurations used in the experiments were supported within this frame. Suitable fluorescent or Lumiline lamps, screened from the observer, illuminated the configurations uniformly. The test elements were seen against the background of a black velvet cloth, which had been stretched tightly over a frame to prevent wrinkles. All details on the cloth, such as lint, which might be seen in binocular vision were also removed, so that the configurations would then be seen against a uniform black, shadowless background. Suitable screens and apertures restricted the field of view of the subject to the area of the fixed frame. The geared unit was suitably mounted before the eyes.

With these experimental conditions, in which insofar as possible, all empiric clues to depth perception are eliminated, measurements of the threshold of the subject to changes in declination principally as a function of stereoscopic acuity are carried out under optimal conditions and can be made with great accuracy. In the majority of the experiments described here, changes in declination and measurements of cyclofusional movements were under 1 degree. Ordinarily cyclotorsions of this magnitude cannot be easily measured with any precision.

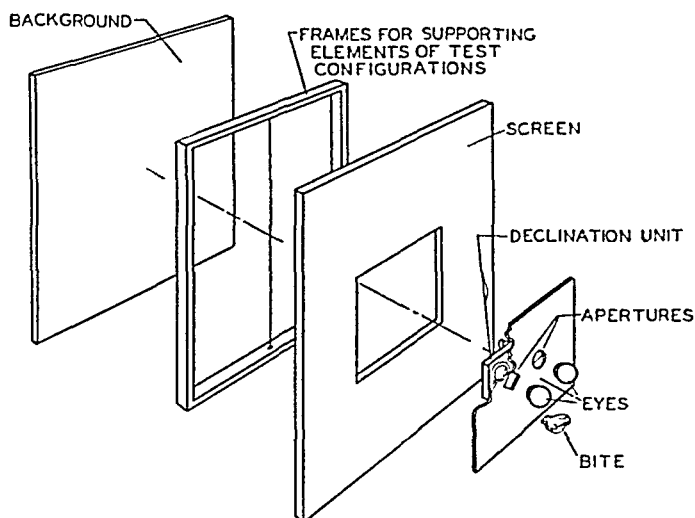


Fig 3—Perspective drawing of the apparatus used

The method of constant stimuli, which is regarded as the most reliable of the three standard psychophysical methods, was used for determining the stereoscopic thresholds, and therefore the sensitivities, in these experiments<sup>23</sup>. This method as applied to the present investigation was as follows. The subject was presented, in a series, a large number of views of the configuration seen through the geared unit, which was set for any one of five steps of change in declination, chosen in random order. These five steps had been selected beforehand within a range of changes in declination at the limits of which the subject always responded correctly. A shutter device when lowered before one eye interrupted binocular observation of the configuration, though a small hole in the shutter permitted binocular fixation at the center. Changes in the declination unit were always made when the shutter was down. During the exposure the subject had only to

<sup>23</sup> For a more detailed description of this method as applied here see a previous article (Stereoscopic Sensitivity to the Space-Eikonometer, *Arch Ophthalm* 34 303-310 [Oct] 1945)

judge whether the configuration was inclined and whether the top was nearer or farther. He was asked to guess if in doubt. Normal ocular movements were permitted while the judgment was being made. The exposure was usually limited to less than two seconds.

From the percentages of the judgments in each category of the change in declination for which the top of the configuration appeared "nearer" (or "farther") a typical psychometric curve was obtained. Examples are shown in figure 4. From this curve, as is customary, the measure of the threshold of the subject to the stimuli is taken as the standard deviation ( $\sigma$ ), which is arrived at by statistical methods.<sup>23</sup> That declination for which 50 per cent of the judgments were "top farther away" and 50 per cent were "top nearer" indicates the most probable declination between the two eyes for which the test configuration appeared truly vertical. At this setting of the geared unit the judgments were pure guesswork, and the distribution found was due solely to chance. At those declination settings

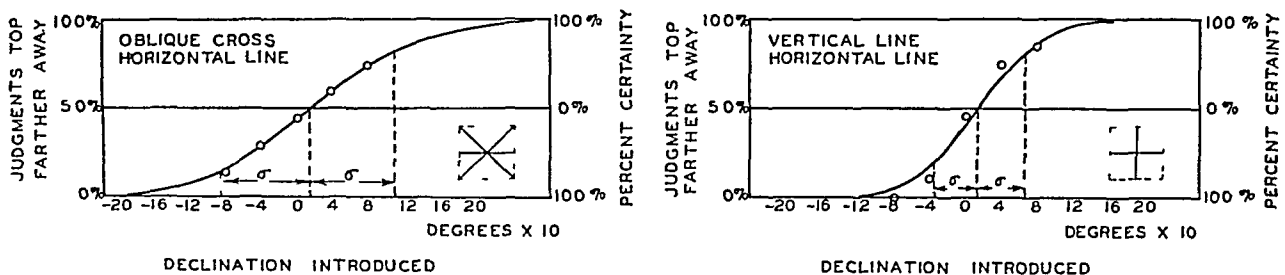
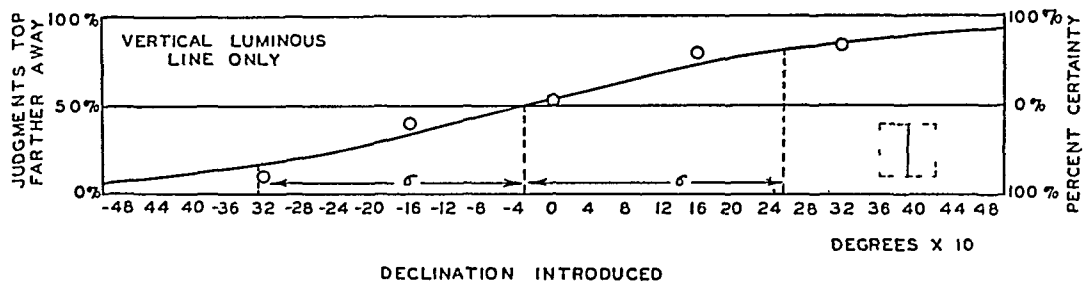


Fig 4—Illustration of typical psychometric curves found in determining the stereoscopic thresholds to changes in declination between the images of the two eyes as seen in an apparent inclination of the test elements in a fore and aft sense, for three different test configurations. Data for V J E

corresponding to the more extreme ends of the curve the subject responded with nearly 100 per cent certainty. Between the declination for the 50-50 point and the declination for the upper limits the proportion of judgments varied from that due chance to near certainty. From this curve, the threshold of response can be read off directly, depending on what percentage of certainty one chooses to consider as the threshold declination.

It must be borne in mind that, while this method of determining thresholds is considered preferable to others, it demands constant attention on the part of the subject and an unvarying criterion of judgment. Moreover, care must be taken that the results are not influenced by such factors as fatigue and distractions.

The six types of combinations of configurations used (a seventh having been studied previously<sup>23</sup>) are illustrated in figure 5. These are (A) two points of light situated vertically, (B) a single vertical line, (C) a vertical line combined

with an oblique cross, (*D*) a vertical line combined with a horizontal line, (*E*) an oblique cross combined with a horizontal line and, finally, (*F*) an oblique cross combined with both a vertical and a horizontal line

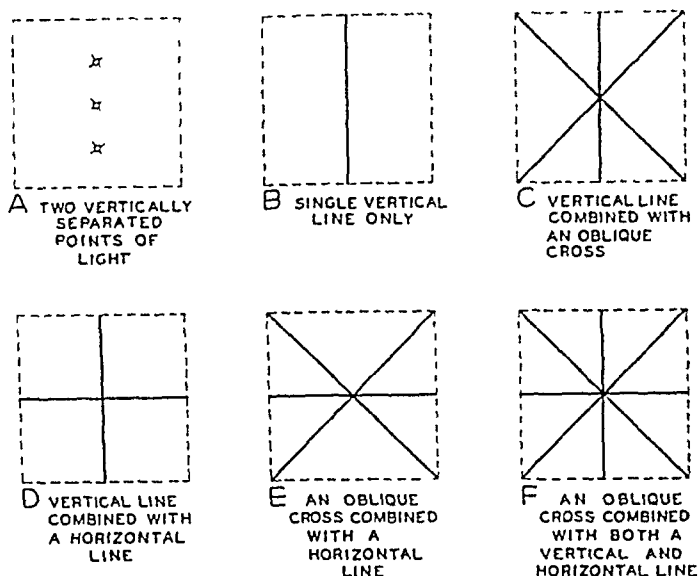


Fig 5—Configurations used in a study of stereoscopic thresholds to changes in declinations between the retinal images of the two eyes and of the influence of cyclofusional movements

*A* represents two vertically separated points of light, *B*, a single vertical line, and *F*, an oblique cross combined with both a vertical and a horizontal line combined with a horizontal line, *E*, an oblique cross combined with a horizontal line, and *F*, an oblique cross combined with both a vertical and a horizontal line

TABLE 1—Results of Experiments to Find Apparent Stereoscopic Thresholds to Changes in Declination Between the Images of the Two Eyes for Various Configurations \*

| Configuration   | Standard Deviations, Degrees |        |       |       |             |
|---|------------------------------|--------|-------|-------|-------------|
|   | V                            | J      | E     | N     | W           |
| A Point sources of light separated vertically 50 cm (range in seven separate experiments) | 0 278                        | 0 560  |       | 0 344 | 0 548       |
| The two point sources combined with a horizontal luminescent line                         | 0 100                        | 0 242* |       | 0 360 | 0 552       |
| B Vertical luminous line only   | 0 270                        | 0 790  |       |       |             |
| Vertical white cord only  | 0 449                        | 0 779  |       |       |             |
| Vertical white rope only  | 0 450                        |        | 0 272 |       | 0 304       |
| C Vertical white rope and oblique cross (white cord)                                      | 0 097                        |        |       |       |             |
| D Vertical white rope and horizontal white rope   | 0 050                        |        | 0 067 |       | 0 059       |
| Vertical white string and horizontal white rope   |                              |        | 0 091 | 0 132 | 0 106-0 110 |
| Vertical white rope and horizontal white string   | 0 048†                       |        | 0 040 |       | 0 040       |
| Vertical white rope and horizontal red string   | 0 019                        |        | 0 066 |       | 0 063       |
| Vertical white rope and horizontal blue thread  | 0 080                        |        | 0 090 |       | 0 104       |
| Vertical white rope and horizontal blue thread strand                                     | 0 128                        |        | 0 137 |       | 0 064       |
| E Oblique white rope cross and horizontal white rope                                      | 0 083                        |        |       |       | 0 074       |
| Oblique white string cross and horizontal white rope                                      | 0 109                        | 0 126  | 0 112 |       | 0 116-0 111 |
| Oblique white thread cross and horizontal white rope                                      | 0 096†                       |        |       |       | 0 079       |
| Oblique white rope cross and horizontal white string                                      | 0 091                        |        |       |       | 0 118       |
| Oblique white rope cross and horizontal white thread                                      | 0 097                        |        |       |       | 0 068       |
| F Vertical white string, oblique white cross, horizontal white rope                       |                              |        |       |       | 0 100       |
| Vertical red string, oblique white cross, horizontal white rope                           | 0 091                        |        |       |       | 0 070       |
| Vertical blue string, oblique red cross, horizontal white rope                            | 0 076                        |        |       |       | 0 106       |

\* The values given are the standard deviations ( $\sigma$ ) in degrees of declination derived from the psychometric data as obtained with the method of constant stimuli

† Psychometric curve is shown in figure 5

## RESULTS

The principal results of the various tests are presented in table 1. Typical psychometric curves for three experiments for one observer are illustrated in figure 4. The results can be summarized as follows:

*A Point Light Sources*—With the room completely darkened, two points of light were arranged vertically (fig. 5A). Each point light source was obtained by adjusting in a suitable housing a small, 6 volt lamp behind a pinhole in a small piece of lead foil. The housings were attached to a vertical rod so that not only would the two point sources be vertical and centered in the frame but their separations could be changed. The lights were adjusted for equal color and brightness. By means of a double throw tap key the two lights could be exposed for only short intervals. When they were not exposed for judgment on the part of the observer, another point source of light in the center would become automatically visible. This light provided a point for binocular fixation when the test stimuli were not exposed.

The results showed the stereoscopic threshold to changes in the declination between the images of the two eyes to be somewhat variable, but on the average it was a little under 0.5 degree. Strangely, however, when a definite declination beyond the midpoint previously found was introduced at the beginning of a series, and the point light sources were continuously observed and ocular movements permitted before the run was begun, it was found that the new psychometric curve obtained was almost identical with the previous curve, with no evidence of the displacement of the midpoint that would be expected. This failure of the curve to shift was early designated a "compensation," either psychologic (a change in the subjective criterion of verticality) or physiologic (a disjunctive cyclotorsion of the eyes). Either change, however, would be for the purpose of keeping the apparent position of the lights vertical. Physiologically, this could only mean that the images are kept nearest corresponding retinal meridians of the two eyes. It is important to point out, however, that this "compensation" did not take place if the change in declination was much greater than  $\pm 1$  degree, for beyond this no psychometric curve could be obtained at all. Nor did this compensation occur consistently without fixating ocular movements during the period of observation. Changing the separation of the points of light from an angular size of 2 degrees to one of 11 degrees did not affect the threshold significantly.

In view of the subsequent experiments, there is little question but that the compensatory effect is due to a cyclofusional movement of the eyes to correct the declination (disparities) between the images and to bring them to corresponding retinal meridians. With each exposure of the points of light for judgment, a compulsion for fusion must

exist, but since the exposure is relatively brief and the cyclofusional movements for such stimuli are slow, it is possible to obtain consistent judgments within a certain range. Obviously, however, with this play, back and forth, during the series of different declinations that were introduced, the apparent stereoscopic threshold of discrimination found would be expected to be relatively high.

*B Single Central Vertical Line*—Substituting a vertical plumb line of either cord or rope for the points of light (fig 5 B) did not materially change the results. The "compensation" effect occurred more easily, but the time of exposure needed for a judgment decreased, and the threshold remained only slightly less than that for the point light sources for all 3 subjects.

*C Vertical Line and Oblique Cross*—By adding to the central vertical line an oblique cross consisting of intersecting white cords attached to the corners of the frame, the situation is stabilized (fig 5 C).

It has been shown geometrically that the apparent inclination of an oblique cross should itself be unaffected by a meridional size lens placed at an oblique axis before one eye.<sup>19c</sup> In these experiments, therefore, changes in the adjustment of the geared unit will not themselves directly affect the orientation of the cross. This follows because equal declinations of the images of the two arms of the cross are introduced by lenses for both eyes.<sup>24</sup> However, a disjunctive cyclotorsion of the two eyes, and therefore of the images with respect to the retinas, would cause the plane of the cross to appear inclined. Thus, in this experiment the apparent inclination of the vertical line relative to the plane of the cross was the criterion of judgment.

The threshold value of the stereoscopic response was reduced to a declination of about 0.1 degree, and little or no "compensation" was found. It is clear that a cyclofusional movement to reduce the declination between the images of the vertical line would introduce declinations on the cross, which, in turn, would constitute stimuli for a movement in the opposite direction. The cross, therefore, stabilizes the movements.

*D A Vertical Line and a Horizontal Line*—Here the cross is removed, and a single horizontal cord is stretched across the frame and used with the vertical cord (fig 5 D). It should be noted that several weights of cords were used for both lines.

With this configuration, it must be remembered that the geared unit introduces a declination between the images of both vertical and horizontal lines, though the images are deviated in opposite directions.

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<sup>24</sup> This follows from the fact that the declinations of the images of any two lines at right angles will be equal but opposite in direction. In the geared unit, these will be equal in the two eyes, and hence the cross will itself be unaffected.<sup>10</sup>

The two compulsions for a cyclofusional movement would, therefore, be antagonistic. If the fusional movement were to offset the horizontal deviation entirely, then the declination between the images of the vertical line would be increased to twice that introduced by the unit itself, and the vertical line should appear inclined nearly twice as much. One would expect, then, the "apparent" threshold of stereoscopic discrimination to be one-half as large as it would if no cyclofusional movement had occurred.

When the subject concentrated his attention on the horizontal line by looking back and forth along it and then made his judgment, the threshold was, indeed, reduced to nearly one half. One must note, however, that there was a tendency for lower "apparent" thresholds with weaker (of less contrast) horizontal lines, indicating that the compulsion for a cyclofusional movement had been reduced. In general, one would expect a compromise between the two stimuli for cyclofusional movements, the resultant depending on the relative degree of contrast and the attention of the subject and, also, on the physiologic "preference" for the correction of one type of declination rather than another.

*E An Oblique Cross and a Horizontal Line*—Here, the oblique cross was substituted for the vertical line and used with the horizontal line (fig 5 E). The subject was again asked to concentrate on the horizontal line and then to judge whether the cross was inclined in space, with the top nearer or farther away. The cross can appear inclined only when a disjunctive cyclotorsion of the images of the two eyes has taken place. Again, the threshold was of the order of 0.1 degree, and this shows that a cyclofusional movement had occurred in the direction of correcting the declination of the images of the horizontal line.

*F Oblique Cross Combined with a Vertical and a Horizontal Line*—A vertical line added to the configuration used in the preceding experiment (fig 5 F) introduced another antagonistic compulsion to fusion. However, the vertical line appeared inclined with respect to the plane of the cross, with a threshold to change in declination of, again, about 0.1 degree. Here, the oblique cross and the horizontal line would dampen any cyclofusional movement to correct the declination of the images of the vertical line, so that the threshold would tend to be uninfluenced by any cyclotorsion.

*Comment*—The proof that the phenomena associated with changes in declination between the images of the two eyes, as they have been described, are due to cyclofusional movements and not to a psychologic change of criterion is in the experiments (1) with the configuration of a vertical and a horizontal line, in which the apparent threshold is



reduced to the order of one half, and (2) with the oblique cross and the horizontal line, in which if the cross appears inclined a cyclotorsion must have taken place

## STEREOSCOPIC PERCEPTION OF INCLINED CONFIGURATIONS AND CYCLOFUSIONAL MOVEMENTS

### INCLINED CONFIGURATIONS

The sensitivity experiments were unsatisfactory in the sense that quantitative information was not found about the specific apparent inclination of a given configuration as influenced by the declination introduced

However, in order that these data may be found, care must be taken as to how the experiments are set up. For example, suppose that within the supporting frame of the instrument an inner wooden frame is mounted so as to be rotatable about a horizontal axis in the plane of this frame and on the level of the subject's eyes. A suitable scale and indicator provide the means for knowing any given inclination of the inner frame. The inclination is taken as positive when the frame inclines back at the top. Within the inner frame a white cord is stretched between the centers of the top and the bottom member, so as to lie in the median plane of the subject and to have the same inclination as the frame. A white cord is then stretched in the axis of rotation of the frame. The configuration is then the same as that shown in figure 5 *D* except that the line which was vertical can now actually be inclined in space. The inclination of the frame can be adjusted by the subject by means of a hand wheel and cords.

The procedure was to introduce a given vertical declination between the images of the two eyes and then have the subject adjust the central cord so that it appeared truly vertical. Whenever possible, the subject was asked to lower the shutter when making the adjustments, so as to eliminate any kinesthetic influence of the moving line. The setting made by the subject was recorded by an assistant. From this inclination, the corresponding declination,  $\delta$ , between the images of the two eyes for this inclination was then calculated from the formula

$$\tan \iota = (2a \tan \delta)/b$$

where, again,  $\iota$  is the angle of inclination,  $2a$  the interpupillary distances and  $b$  the visual distance

Table 2 and figure 6 illustrate typical data obtained for the  $\delta$ , calculated from the inclination of the line which appears vertical for various declinations introduced. In the figure, the declination measured is plotted on the ordinate, and the declination introduced by the geared unit, on the abscissa. It will be noted that the measured declination from the inclined line is twice that introduced. Clearly, then, cyclo-

TABLE 2—Typical Data\* Showing a Cyclofusional Movement of the Eyes Due to the Compulsion to Fusion on a Horizontal Line When Declinations Are Introduced by Meridional Size Lenses

| Declination Introduced,<br>Degrees<br>( $\delta_u$ ) | Inclination<br>of Line, Degrees<br>( $i$ ) | Equivalent Declination<br>(Computed), Degrees<br>( $\delta_m$ ) |
|--|--|---|
| +0 84  | —40 7                                      | —1 52   |
| +0 67  | —28 3                                      | —0 99   |
| +0 51  | —20 0                                      | —0 66   |
| +0 34  | —12 3                                      | —0 39   |
| +0 17  | — 2 0                                      | —0 06   |
| 0 00   | + 4 5                                      | +0 14   |
| 0 00   | + 7 8                                      | +0 25   |
| —0 17  | +17 4                                      | +0 57   |
| —0 34  | +25 4                                      | +0 85   |
| —0 51  | +33 7                                      | +1 20   |
| —0 67  | +39 1                                      | +1 46   |

\* The values are the degrees through which a line must be inclined fore and aft in space to appear truly vertical (data obtained from K N O)

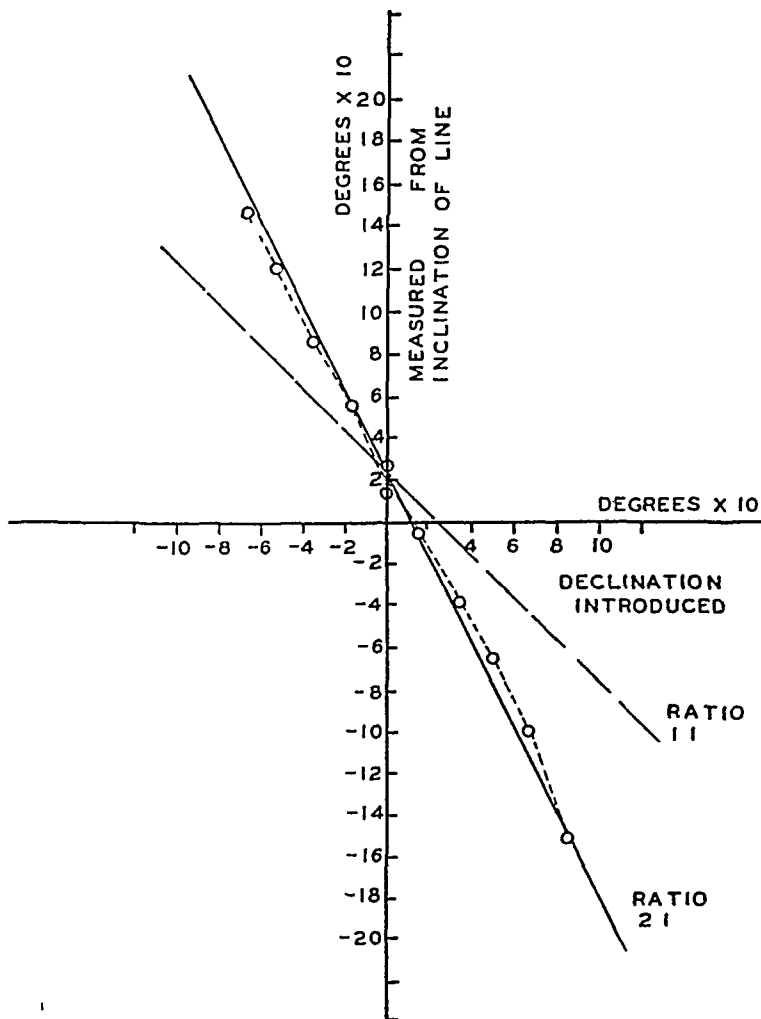


Fig 6—Typical data from the inclination of a vertical line in space adjusted for the apparent stereoscopic vertical when declinations between the retinal images of the two eyes are introduced by optical means. The 2 1 ratio indicates that cyclofusional movements have occurred which entirely eliminate the declination between the retinal images for a horizontal line.

fusional movements must have occurred to eliminate entirely the declination between the images of the horizontal line. However, when the central line appeared vertical there would be no declination between its images in the two eyes, and hence it would exert no antagonistic compulsion to fusion.

While interesting, this experiment does not tell what the cyclofusional movement would be on the vertical and the horizontal line when a declination on each is introduced by the geared unit, for, obviously, as the line is inclined to appear vertical in the experiment the compulsion to fuse the declination between its images decreases and the only compulsion is exerted by the horizontal line. One would anticipate, therefore, a 2:1 ratio between the declination measured and that indicated by the drum on the geared unit.

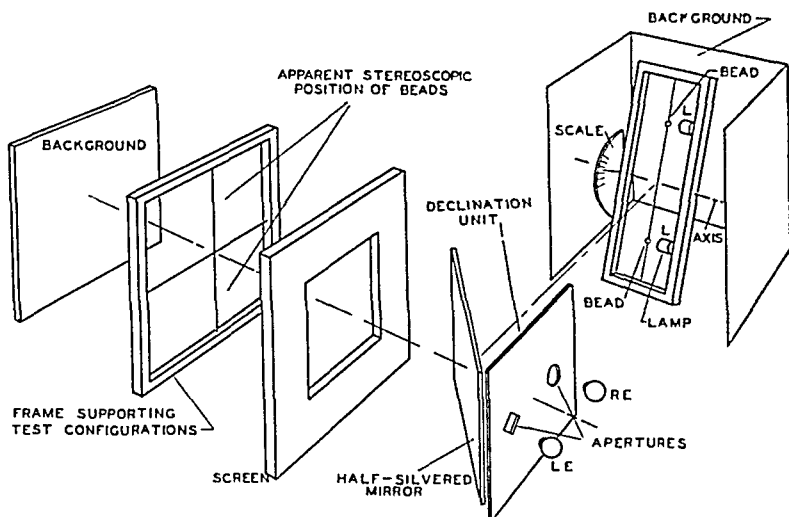


Fig 7—Perspective drawing of modified apparatus showing a bead device, by which the apparent stereoscopic vertical could be determined

The problem, then, was to find a device which would permit one to establish the apparent stereoscopic vertical (stereovertical) in a given experiment without that device itself introducing a measurable compulsion to cyclofusional movements. It was found that two separated pearl beads on a black thread attached in the rotatable frame previously described might be used. However, even the black thread itself was visible in many positions of the frame, and this was found to exert a compulsion for a cyclofusional movement.

The apparatus was therefore enlarged, so that the beads would be seen by reflection in a half-silvered mirror set up in front of the declination unit (fig 7). The beads were supported on a black thread attached to the top and bottom of a narrow wooden frame, which was pivoted so as to rotate about a horizontal axis at the level of the subject's eyes.

The distance of this frame was such that the images of the beads were seen stereoscopically at the same distance as the distance of the frame supporting the test elements of the apparatus. The beads were independently illuminated and seen against a black background. If the experiments were conducted in a half-darkened room, the thread supporting the beads could not be seen. As compared with most of the test configurations used, the beads themselves exerted only an insignificant compulsion for cyclofusional movements.

To reduce further a possible compulsion to fusion on the beads, a timing device was placed in the electrical circuit of the lamps so that the beads would be seen intermittently for only a second at a time, with a one second "off" interval. By means of a hand wheel and cords, the subject could adjust the inclination of the frame and therefore that of the beads. As before, the angle of inclination was taken as positive when the beads were inclined back (away) at the top, in order that the corresponding declinations of the images in the two eyes would be positive. The test configurations themselves (except where noted) were then fixed vertically in the central frame.

The procedure in a given experiment was simply to introduce a declination between the images of the two eyes by means of the geared unit<sup>25</sup> and to instruct the subject to turn the hand wheel to adjust the beads until they appeared vertical (or, what is equivalent in this case, equally distant from him). The actual inclination of the cord supporting the beads was then read from the scale attached to the frame. From this measurement the equivalent declination was then computed, as previously indicated.

The suitability and precision of the technic of using the beads in this modified apparatus are shown in three fundamental experiments. First, a single horizontal line only is used. The declination unit introduces equal declinations, though opposite in direction, in the vertical and the horizontal meridian. If no cyclofusional movement occurs to reduce or eliminate the declination of the images of the horizontal line, then the actual inclination of the beads should only be such as to offset the vertical declination introduced by the geared unit. If, however, a cyclofusional movement of the eyes does occur and eliminates the declination of the images of the horizontal line, then the actual inclination of the beads should be such as to offset twice the declination between the images for the vertical meridian. The results, as shown in table 3 and figure 8, show that this cyclofusional movement has occurred to the full extent.

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<sup>25</sup> It was often noted that if one observed a configuration when a declination had been introduced the subjective impression was that the vertical contours were vertical. But when the beads were then adjusted so that they appeared vertical, these contours appeared definitely inclined.

In the figure, the declination angle introduced by the geared unit is plotted on the abscissa, while along the axis of ordinates are plotted the corresponding declinations between the images of the two eyes

TABLE 3—*Typical Set of Data Showing the Measured Vertical Declination Between the Images of the Two Eyes as Measured by the Inclination at Which Two Separated Beads Were Set so as to Appear Vertical When Declinations Were Introduced Between the Images*

| Declination Introduced, Degrees ( $\delta_a$ ) | Horizontal Line Only          |   | Vertical Line Only            |   | Oblique Cross Only            |   |
|--|-------------------------------|---|-------------------------------|---|-------------------------------|---|
|  | Inclination of Beads, Degrees | Corresponding Declination, Degrees ( $\delta_b$ ) | Inclination of Beads, Degrees | Corresponding Declination, Degrees ( $\delta_i$ ) | Inclination of Beads, Degrees | Corresponding Declination, Degrees ( $\delta_b$ ) |
| +0 80  | -42 1 $\pm$ 1 7               | -1 56   | -2 2 $\pm$ 0 1                | -0 06   | -25 5 $\pm$ 0 8               | -0 78   |
| +0 60  | -31 6 $\pm$ 0 7               | -1 06   | -1 7 $\pm$ 0 2                | -0 04   | -18 7 $\pm$ 0 7               | -0 55   |
| +0 40  | -21 7 $\pm$ 1 1               | -0 67   | -1 0                          | -0 05   | -11 3 $\pm$ 1 1               | -0 33   |
| +0 20  | -10 9 $\pm$ 1 2               | -0 32   | -2 3 $\pm$ 0 5                | -0 06   | -5 2 $\pm$ 0 3                | -0 15   |
| -0 20  | +13 1 $\pm$ 0 4               | +0 39   | -1 7 $\pm$ 0 1                | -0 04   | +5 9 $\pm$ 0 1                | -0 17   |
| -0 40  | +21 2 $\pm$ 0 8               | +0 65   | +1 5 $\pm$ 1 3                | +0 04   | +11 6 $\pm$ 2 0               | +0 33   |
| -0 60  | +34 2 $\pm$ 1 1               | +1 17   | +3 0 $\pm$ 2 2                | +0 09   | +20 3 $\pm$ 0 5               | +0 61   |
| -0 80  | +41 3 $\pm$ 0 7               | +1 62   | +6 1 $\pm$ 1 1                | +0 17   | -25 9 $\pm$ 0 6               | +0 79   |

\* Data for K N O, visual distance, 22 meters

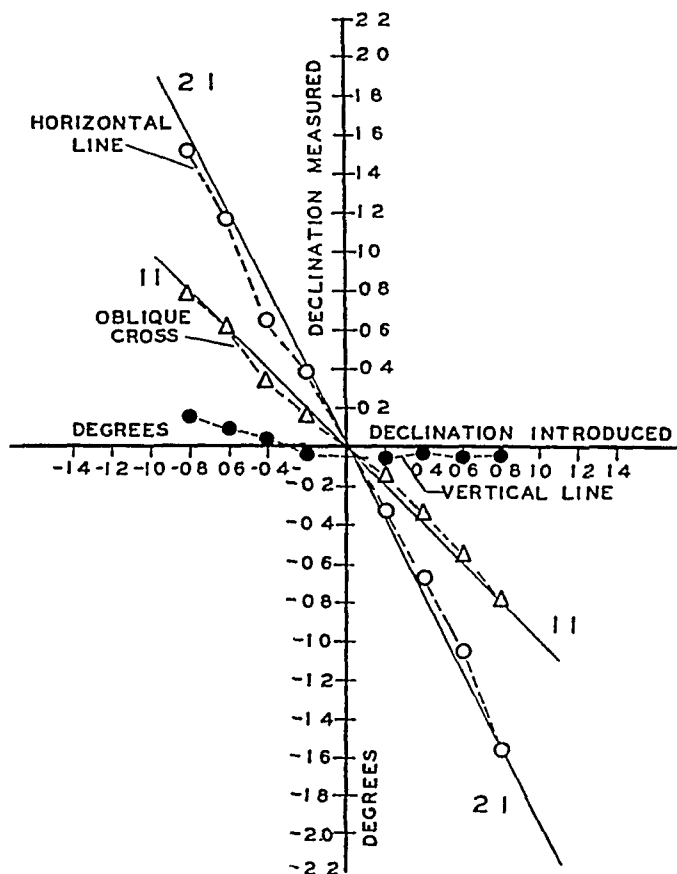


FIG 8—Typical results obtained for the three fundamental experiments using the beads as a means of determining the spatial inclination for the apparent stereoscopic vertical

determined from the actual inclination of the beads for which they appeared vertical

Second, a vertical cord only is used as the test configuration. Again, the beads, which are seen a little to one side of the line, are adjusted by the subject for the apparent vertical. The actual inclination of the beads will be different, depending on whether or not a cyclofusional movement has occurred. If no fusional movement has taken place, the line should appear inclined in space because of the vertical declination that has been introduced. The inclination of the beads should then be such as to offset the vertical declination introduced. On the other hand, if there is a cyclofusional movement such as to eliminate

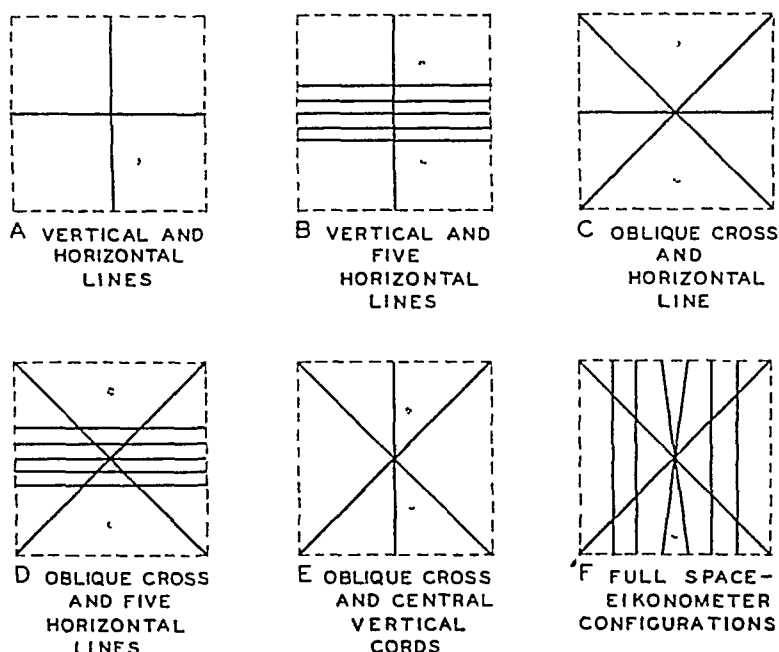


Fig 9—Configurations used as binocular fusional stimuli for studying cyclofusional movements in response to declinations introduced between the images of the two eyes by optical means. The small circles of interrupted lines indicate the approximate position of images of beads as seen by the subject.

*A* consists of a vertical and a horizontal line, *B*, of a vertical and five horizontal lines, *C*, of an oblique cross and a horizontal line, *D*, of an oblique cross and five horizontal lines, *E*, of an oblique cross and a central vertical cord, and *F*, full space eikonometer configurations.

entirely the vertical declination introduced, the line should appear vertical, and the actual inclination of the beads should be zero. The latter is shown to be the case, except for a suggestion that when negative declinations are introduced the cyclofusional movement is not quite complete.

Third, an oblique cross consisting of white cords attached to the corners of the frame is used as the test configuration. With this configuration, a 1:1 ratio would be expected between the measured  $\delta_b$  from the setting of the beads and the vertical declination  $\delta_a$  introduced, because the geared unit does not itself affect the apparent orientation.

of the oblique cross. As shown by table 3 and figure 8, the measured declinations associated with the beads are substantially equal to the declinations introduced.

These results indicate that with a single stimulus for cyclofusional movement, that movement occurs practically completely in the interest of single binocular vision and, therefore, for the purpose of making the retinal images in the two eyes fall as nearly as possible on meridians corresponding to the stereoscopic vertical.

#### CYCLOFUSIONAL MOVEMENTS

More important now is the answer to the question how the eyes respond to stimuli for fusional movements which are antagonistic. The studies described in the following section seek to answer that question.

*Vertical and Horizontal Lines*—This configuration consists of vertical and horizontal strings attached to the sides of the central frame (fig. 9A). As already pointed out, a setting of the geared unit introduces equal but opposite declination between the images of the two eyes for the vertical and the horizontal meridian (fig. 2). Each of the elements of this configuration, therefore, provides a stimulus for a cyclofusional movement in an opposite direction. If each exerted the same compulsion, no torsion would result. However, in general, it was found that there was a cyclofusional movement in the direction to decrease the declination between the images of the vertical element.

The inclination of the beads will always provide the measure for the resultant declination of the images of the vertical elements. Hence, if a vertical declination of  $\delta_u$  degrees is introduced by the geared unit, and subsequently a cyclofusional movement of  $\tau$  degrees occurs, the resultant vertical declination between the images would be  $(\delta_u - \tau)$ . Here,  $\tau$  is taken as positive for an excyclotorsion and as negative for an incyclotorsion. The beads will then have to be inclined in space if they are to appear vertical, so that the vertical declination they introduce,  $\delta_b$ , will offset the resultant declination. One has, then,  $\delta_b = -(\delta_u - \tau)$ , and hence the cyclotorsion  $\tau$  between the eyes will be  $\tau = \delta_b + \delta_u$ .

In table 4 and figure 10, typical data for this configuration are given. The one set of data is for the single vertical and horizontal strings, showing that cyclofusional movements to the extent of 60 per cent have occurred to correct the vertical declination. If more horizontal lines with greater contrast, such as white rope, replace the single horizontal cord (fig. 9B), the cyclofusional movement is significantly less, showing that the compulsion for fusion on the horizontal strings has now been increased. However, the compulsion from the vertical strings is still strong enough to cause an actual cyclofusional movement.

Attempts were made to influence the degree of cyclofusional movements by having the subject concentrate his attention on the vertical or the horizontal elements. However, no significant differences in the results were found in this case.

TABLE 4—*Typical Data Showing Degree of Cyclofusional Movements Associated with Configurations of Vertical and Horizontal Lines When Equal but Opposite Declinations Are Introduced Between the Images of Those Lines\**

| Vertical and Horizontal Cord                   |                                       |  |  | Vertical Cord with Five Horizontal Ropes |  |  |
|--|---------------------------------------|--|--|--|--|--|
| Declination Introduced, Degrees ( $\delta_a$ ) | Inclination of Beads, Degrees ( $i$ ) | Corresponding Declinations, Degrees ( $\delta_b$ ) | Total Cyclotorsion of Eyes, Degrees ( $\tau$ ) | Inclination of Beads, Degrees ( $i$ )    | Corresponding Declinations, Degrees ( $\delta_b$ ) | Total Cyclotorsion of Eyes, Degrees ( $\tau$ ) |
| +0 80  | -15 1                                 | -0 45  | +0 35  | -15 4                                    | -0 46  | +0 34  |
| +0 60  | -7 9                                  | -0 24  | +0 46  | -12 7                                    | -0 38  | +0 22  |
| +0 40  | -5 5                                  | -0 17  | +0 23  | -7 8                                     | -0 23  | +0 17  |
| +0 20  | -2 8                                  | -0 09  | +0 11  | -4 9                                     | -0 14  | +0 06  |
| -0 20  | +0 1                                  | +0 01  | -0 19  | +3 2                                     | +0 10  | -0 10  |
| -0 40  | +3 2                                  | +0 12  | -0 28  | +8 2                                     | +0 24  | -0 16  |
| -0 60  | +8 9                                  | +0 26  | -0 34  | +16 1                                    | +0 48  | -0 12  |
| -0 80  | +12 4                                 | +0 36  | -0 44  | +20 3                                    | +0 62  | -0 18  |

\* Data for K N O

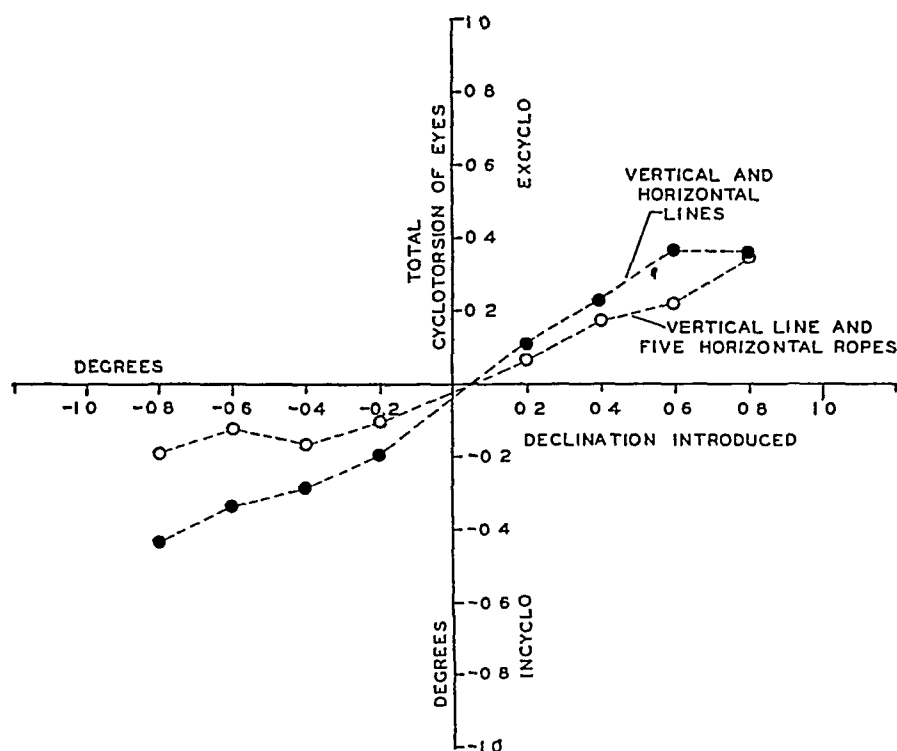


Fig 10—Results which show that the compulsion for a cyclofusional movement is greater for declinations between images of vertical lines than for declinations between images of horizontal lines of the same weight. When more horizontal contours are added, this cyclofusional movement is reduced.

There was other evidence that the compulsion for a cyclofusional movement exerted by the vertical contours was not only stronger than that exerted by the horizontal but much faster. A series of settings



of the beads made at intervals of about fifteen seconds showed that in the beginning the cyclotorsion was actually greater for the vertical line (almost complete at times) and that as the settings were continued the magnitude of the cyclotorsion in that direction decreased, i. e., a cyclofusional movement toward the horizontal increased, finally reaching a stable value. Even these values might vary somewhat over a prolonged period of observation.

This phenomenon of a stronger and faster compulsion to fusion caused by declinations of the images of vertical contours than by declinations of images of horizontal contours, in spite of stereopsis, is noteworthy not only for its own sake but because it is not consistent with accepted notions, at least regarding fusional movements in the visual plane. There the evidence was that contours whose retinal images were disparate excited involuntary compulsions to fusion only when not seen in stereoscopic depth.

*A Horizontal Element and an Oblique Cross*—When an oblique cross consisting of cords stretched between the corners of the frame is substituted for the vertical line used in (fig. 9 C) in the preceding experiment, the stimulus for a cyclofusional movement can arise only from the horizontal contour (since the cross is unaffected by the geared unit). The settings of the beads in this experiment proved unusually difficult as compared with the previous experiments because the great subjective uncertainty of each setting proved disturbing, and even frustrating.

If a cyclofusional movement does occur to decrease or eliminate the declination between the image of the horizontal contours, then the oblique cross should appear inclined in space. The magnitude of this inclination,  $\iota_c$ , is related to the amount of cyclotorsion,  $\tau$ , by <sup>19c</sup>

$$\tan \iota_c = -\frac{b}{a} \tan \tau$$

where, as before,  $b$  is the visual distance and  $2a$  is the interpupillary separation,  $b$  being large as compared with  $a$ ,  $\tau$  will be positive for an excyclotorsion and negative for an incyclotorsion of the eyes. The inclination,  $\iota_c$ , will be positive when the top of the cross appears farther away and negative when it appears nearer. It is clear that this inclination is roughly twice that of a vertical line for the equivalent declination between the retinal images.

In this experiment the beads could be adjusted for two criteria (1) the apparent vertical and (2) the same apparent inclination of the plane of the cross. The cyclotorsion can be determined from either measurement. As previously outlined, from the inclination of the beads for the apparent vertical, the cyclotorsion would be given by  $\tau = \delta_u + \delta_b$ . When the beads are adjusted so that they have the same apparent inclination,  $\iota_c$ , as has the cross, one can write (from

equations 1 and 3) that if  $\delta_{bc}$  denotes the declination corresponding to the inclination of the beads

$$\tan \iota_c = -\frac{b}{a} \tan \tau = \frac{b}{2a} (\tan \delta_u - \tan \tau + \tan \delta_{bc})$$

Remembering that the angles  $\delta$  and  $\tau$  are small, one obtains for the cyclotorsion,  $\tau = -(\delta + \delta_{bc})$ . From these two formulas, it is clear that  $\delta_u = -(\delta_b + \delta_{bc})$ . This last relation provides a check on the consistency of the data when both criteria are used, and the values obtained will indicate the degree to which a change in the cyclotorsion has occurred between the two parts of the experiment according to the two criteria

TABLE 5—Data Showing Increased Cyclotorsional Movements Associated with Increased Number of Horizontal Contours \*

| Declination<br>Introduced,<br>Degrees      | Setting Beads for<br>Apparent Vertical |                              |                               | Setting Beads for<br>Same Apparent Inclination<br>as That of Cross |                              |                               | Con-<br>sistency<br>Check,<br>Degrees | Average<br>Cyclo-<br>torsion,<br>Degrees |              |             |                 |
|--|--|------------------------------|-------------------------------|--|------------------------------|-------------------------------|---------------------------------------|--|--------------|-------------|-----------------|
|  | Inclina-<br>tion,<br>Degrees           | Declina-<br>tion,<br>Degrees | Cyclo-<br>torsion,<br>Degrees | Inclina-<br>tion,<br>Degrees                                       | Declina-<br>tion,<br>Degrees | Cyclo-<br>torsion,<br>Degrees |                                       |  |              |             |                 |
|  |  |                              |                               |  |                              |                               |                                       |  | $\tau =$     | $\tau =$    | $\tau =$        |
|  |  |                              |                               |  |                              |                               |                                       |  | $(\delta_u)$ | $(\iota_v)$ | $(\delta_{bv})$ |
| I Oblique Cross and Horizontal Lane        |  |                              |                               |  |                              |                               |                                       |  |              |             |                 |
| +0 80                                      | -23 9                                  | -0 72                        | +0 08                         | -23 1  | -0 70                        | -0 10                         | +0 71                                 | -0 01                                    |              |             |                 |
| +0 60                                      | -20 8                                  | -0 62                        | -0 02                         | -14 9  | -0 44                        | -0 16                         | +0 53                                 | -0 09                                    |              |             |                 |
| +0 40                                      | -18 2                                  | -0 54                        | -0 14                         | -13 3  | -0 39                        | -0 01                         | +0 46                                 | -0 07                                    |              |             |                 |
| +0 20                                      | -10 4                                  | -0 30                        | -0 10                         | -3 8   | -0 11                        | -0 09                         | +0 20                                 | -0 09                                    |              |             |                 |
| -0 20                                      | + 6 6                                  | +0 19                        | -0 01                         | +10 3  | +0 29                        | +0 09                         | -0 24                                 | +0 04                                    |              |             |                 |
| -0 40                                      | +17 2                                  | +0 50                        | +0 10                         | +14 7  | +0 43                        | -0 03                         | -0 47                                 | +0 03                                    |              |             |                 |
| -0 60                                      | +20 0                                  | +0 60                        | 0 0                           | +20 8  | +0 62                        | -0 02                         | -0 61                                 | -0 01                                    |              |             |                 |
| -0 80                                      | +24 4                                  | +0 74                        | -0 06                         | +27 0  | +0 83                        | -0 03                         | -0 78                                 | -0 05                                    |              |             |                 |
| II Oblique Cross and Five Horizontal Lines |  |                              |                               |  |                              |                               |                                       |  |              |             |                 |
| +0 80                                      | -38 0                                  | -1 31                        | -0 51                         | -3 0   | -0 09                        | -0 71                         | +0 70                                 | -0 61                                    |              |             |                 |
| +0 60                                      | -31 4                                  | -1 0                         | -0 40                         | -3 7   | -0 11                        | -0 49                         | +0 56                                 | -0 45                                    |              |             |                 |
| +0 40                                      | -23 7                                  | -0 70                        | -0 30                         | -4 0   | -0 12                        | -0 18                         | +0 41                                 | -0 24                                    |              |             |                 |
| +0 20                                      | -15 7                                  | -0 46                        | -0 26                         | -0 35  | -0 01                        | -0 19                         | +0 23                                 | -0 22                                    |              |             |                 |
| -0 20                                      | +13 7                                  | +0 40                        | +0 20                         | -0 1   | -0 01                        | +0 21                         | -0 20                                 | +0 20                                    |              |             |                 |
| -0 40                                      | +22 6                                  | +0 68                        | +0 28                         | -2 0   | -0 06                        | +0 46                         | -0 37                                 | +0 37                                    |              |             |                 |
| -0 60                                      | +26 3                                  | +0 81                        | +0 21                         | +3 6   | +0 10                        | +0 50                         | -0 46                                 | +0 45                                    |              |             |                 |
| -0 80                                      | +27 0                                  | +0 83                        | +0 03                         | +8 0   | +0 24                        | +0 56                         | -0 53                                 | +0 29                                    |              |             |                 |

\* Data on V J E

Table 5 gives the typical data for 1 subject. These are also illustrated in figure 11. For this subject, substantially no significant cyclofusional movement occurred in any part of the experiment with the oblique cross and the horizontal line. Thus, it is clear in this case that the compulsion for a cyclofusional movement is not sufficient to counterbalance the compulsions that would be introduced by the disparate images of the lines of the oblique cross.

If, however, five horizontal heavy white ropes are substituted for the single horizontal cord (fig 9D), significantly large cyclofusional movements do occur which for the small declinations introduced are sufficient to eliminate completely the declinations of the images of the horizontal elements. Thus, as soon as the number and contrast of

the horizontal contours are increased, the compulsion arising from the declinations of these contours becomes great enough to offset entirely the opposing compulsions that arise from the oblique cross, and then a torsion takes place

*A Vertical Element and an Oblique Cross*—Consider, now, an oblique cross in combination with vertical elements in the plane of the cross. These vertical elements may consist of a single vertical cord (fig 9 E), two separated vertical cords or two cords crossed at a very acute angle, as shown in the center of figure 9 F. When the geared unit is now used to introduce declinations, the cross itself will not be affected, but declinations will be introduced between the images of the vertical elements. The extent to which a cyclofusional movement will now occur depends on the relative compulsions of the vertical contours as opposed to those of the oblique cross. With the procedure

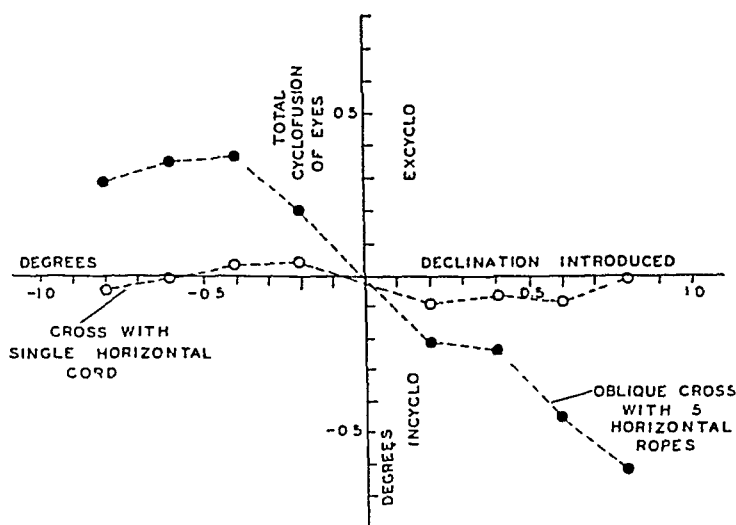


Fig 11—Results which show that only when the number of horizontal contours is increased will the compulsion for a cyclofusional movement offset the stabilizing effect of an oblique cross

previously outlined, data were obtained according to the two criteria. Table 6 gives typical results, which are also illustrated in figure 12. These results show that cyclofusional movements do occur in every case, and their magnitude is about the same for any one of the types of vertical elements.

However, if the central vertical elements are placed in front of the plane of the cross, so that their images, as compared with the images of the cross, now have horizontal disparities, the cyclofusional movements are greatly reduced. In the experiment in which the two vertical cords are 40 cm in front of the cross, practically no cyclo-torsion takes place. Typical data are also shown in figure 12. Thus, as might be anticipated, the compulsion for cyclofusional movements

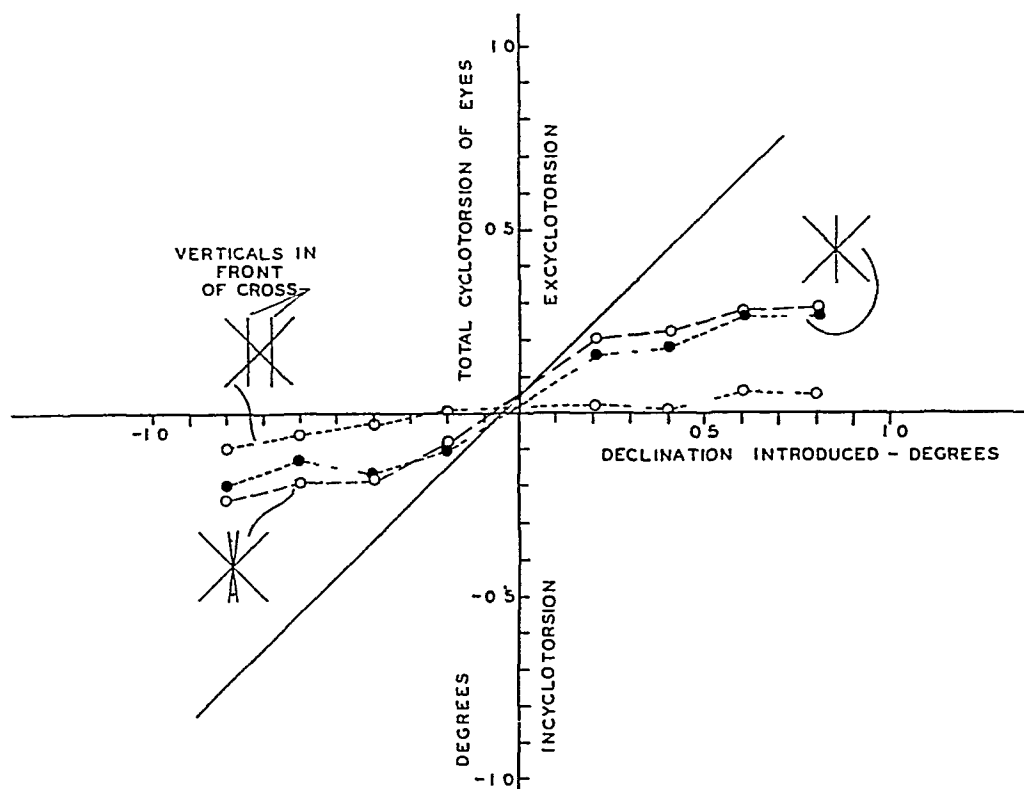


Fig 12—Results which show that the compulsion for cyclofusional movements from images of vertical contours is greater than that from the oblique cross. When horizontal disparities are introduced between the images of vertical contours, the compulsion of those images to cyclofusional movements decreases

TABLE 6—Data Showing Degree of Cyclofusional Movements Associated with Vertical Contours Against the Stabilizing Contours of the Oblique Cross\*

| Declination Introduced, Degrees                                     | Setting Beads for Apparent Vertical |                      |                        | Setting Beads for Same Apparent Inclination as That of Cross |                      |                        | Consistency Check, Degrees                                       | Average Cyclo-torsion, Degrees |
|---|-------------------------------------|----------------------|------------------------|--|----------------------|------------------------|--|--------------------------------|
|   | Inclination, Degrees                | Declination, Degrees | Cyclo-torsion, Degrees | Inclination, Degrees   | Declination, Degrees | Cyclo-torsion, Degrees |  |                                |
| ( $\delta_u$ )  | ( $\iota_v$ )                       | ( $\delta_{bv}$ )    | ( $\tau$ )             | ( $\iota_v$ )  | ( $\delta_{bc}$ )    | ( $\tau$ )             | $-\frac{1}{2}(\delta_{bv} + \delta_{bc})$<br>( $= \delta_{bu}$ ) | ( $\tau$ )                     |
| I Oblique Cross and Single Vertical Cord in Plane of Cross          |                                     |                      |                        |  |                      |                        |  |                                |
| +0 80   | -16 6                               | -0 49                | +0 31                  | -31 8  | -1 01                | +0 21                  | +0 75  | +0 26                          |
| +0 60   | -10 7                               | -0 31                | +0 29                  | -27 9  | -0 86                | +0 26                  | +0 58  | +0 27                          |
| +0 40   | -7 0                                | -0 20                | +0 20                  | -18 8  | -0 55                | +0 15                  | +0 38  | +0 18                          |
| +0 20   | -2 5                                | -0 07                | +0 13                  | -13 8  | -0 40                | +0 20                  | +0 23  | +0 16                          |
| -0 20   | +4 3                                | -0 13                | -0 07                  | +11 7  | +0 34                | -0 14                  | -0 23  | -0 10                          |
| -0 40   | +6 9                                | +0 20                | -0 20                  | +18 4  | +0 54                | -0 14                  | -0 37  | -0 17                          |
| -0 60   | +15 1                               | +0 45                | -0 15                  | +23 9  | +0 72                | -0 12                  | -0 63  | -0 13                          |
| -0 80   | +17 3                               | +0 51                | -0 29                  | +29 5  | +0 92                | -0 12                  | -0 71  | -0 20                          |
| II Oblique Cross and Two Crossed Central Cords in Plane of Cross    |                                     |                      |                        |  |                      |                        |  |                                |
| +0 80   | -13 1                               | -0 38                | +0 42                  | -29 9  | -0 94                | +0 14                  | +0 76  | +0 28                          |
| +0 60   | -9 8                                | -0 28                | +0 32                  | -27 0  | -0 83                | +0 23                  | +0 56  | +0 27                          |
| +0 40   | -4 7                                | -0 14                | +0 26                  | -19 5  | -0 58                | +0 18                  | +0 36  | +0 22                          |
| +0 20   | -2 3                                | -0 07                | +0 13                  | -10 6  | -0 47                | +0 27                  | +0 27  | +0 20                          |
| -0 20   | +6 0                                | +0 17                | -0 03                  | +11 9  | +0 34                | -0 14                  | +0 26  | -0 03                          |
| -0 40   | +9 2                                | +0 27                | -0 13                  | +17 6  | +0 52                | -0 12                  | +0 39  | -0 18                          |
| -0 60   | +11 1                               | +0 33                | -0 27                  | +23 9  | +0 72                | -0 12                  | +0 53  | -0 19                          |
| -0 80   | +13 2                               | +0 38                | -0 42                  | +28 1  | +0 87                | -0 07                  | +0 63  | -0 24                          |
| III Oblique Cross and Two Vertical Cords in Front of Plane of Cross |                                     |                      |                        |  |                      |                        |  |                                |
| +0 80   | -26 2                               | -0 81                | -0 01                  | -29 4  | -0 91                | +0 11                  | +0 96  | +0 05                          |
| +0 60   | -21 5                               | -0 64                | -0 04                  | -25 8  | -0 78                | +0 18                  | +0 71  | +0 06                          |
| +0 40   | -14 5                               | -0 42                | -0 02                  | -14 9  | -0 43                | +0 03                  | +0 42  | +0 01                          |
| +0 20   | -6 5                                | -0 18                | -0 02                  | -6 6   | -0 17                | +0 03                  | +0 18  | +0 02                          |
| -0 20   | +6 1                                | +0 18                | -0 02                  | +4 3   | -0 13                | +0 07                  | -0 16  | +0 02                          |
| -0 40   | +11 6                               | +0 34                | -0 06                  | +17 5  | +0 52                | -0 12                  | -0 43  | -0 03                          |
| -0 60   | +17 2                               | +0 50                | -0 10                  | +20 9  | +0 62                | -0 02                  | -0 56  | -0 06                          |
| -0 80   | +24 7                               | +0 75                | -0 05                  | +30 5  | +0 96                | -0 16                  | -0 85  | -0 10                          |

\* Data for V J E

resulting from declinations of the images of vertical contours is reduced if horizontal disparities are also introduced between their images in the two eyes

On the other hand, if pairs of vertical cords are placed both before and behind the plane of the cross (as in the case of the space eikonometer), cyclofusional movements will occur

In figure 12 are also illustrated the typical results of the degree of cyclofusional movements that occur with the complete configuration of test elements as used in the space eikonometer (cf fig 9*F*). It would appear that these movements are not much greater with the four vertical cords than are those found with the central vertical elements in the plane of the cross

*Vertical and Inclined Contours*—Cyclofusional movements also occur when both vertical and inclined contours only are present in the field of view

If the outer two of three vertical lines (in the objective fronto-parallel plane) in space are inclined with their tops nearer the observer and the entire binocular visual field is restricted to these lines, it will be seen that the central line, instead of appearing vertical, as it is, appears inclined somewhat back at the top. Werner<sup>26</sup> described this phenomenon as observed in a stereoscope and designated it a "binocular depth contrast" phenomenon

Within the central frame of the apparatus a separate square frame was fixed so that it could be rotated about a horizontal axis and could be adjusted for any angle of inclination. Within both the fixed and the movable frame various configurations of cords could be fastened. Six configurations were used: (1) two separated cords, one of which was vertical and the other could be inclined, (2) one central vertical cord and two outer cords which could be inclined, (3) the same configuration as that designated in (2) except that a horizontal cord was added, (4) two vertical cords and a central cord which could be inclined, (5) a central vertical cord and eight cords, four on a side, which could be equally inclined, and (6) eight vertical cords and one cord which could be inclined. The geared unit was set at zero and was not used. Obviously, the purpose of these different configurations was to get various degrees and types of compulsions for cyclofusional movements. Throughout the experiments the beads were used to determine that inclination which corresponded to the criterion of the subjective vertical. The inclination of the beads when the two appeared vertical would give a direct measure of the degree of cyclo-torsion the eyes had undergone, since the geared unit was not used

26 Werner, H. Binocular Depth Contrast and the Conditions of the Binocular Visual Field, *Am J Psychol* 51: 489-497, 1938

Table 7 gives the data for 1 subject. The data are also illustrated graphically in figure 13. A study of the data thus presented shows clearly that a cyclofusional movement generally takes place except when the number of contours which could give rise to antagonistic compulsions are greatly increased.

TABLE 7—*Typical Data Showing Existence of Cyclofusional Movements in Various Combinations of Vertical and Inclined Lines\**

| Inclination of Elements |              | Two Lines, One Inclined |                | Three Lines, Outer Inclined |                | Three Lines, Inner Inclined |                | Nine Lines, All But Center Inclined |                | Nine Lines, Only Center Inclined |                |
|-------------------------|--------------|-------------------------|----------------|-----------------------------|----------------|-----------------------------|----------------|-------------------------------------|----------------|----------------------------------|----------------|
| ( $\iota$ )             | ( $\delta$ ) | ( $\iota_b$ )           | ( $\delta_b$ ) | ( $\iota_b$ )               | ( $\delta_b$ ) | ( $\iota_b$ )               | ( $\delta_b$ ) | ( $\iota_b$ )                       | ( $\delta_b$ ) | ( $\iota_b$ )                    | ( $\delta_b$ ) |
| +40                     | +1.46        | +20.9                   | +0.63          | +20.2                       | +0.94          | +2.1                        | +0.06          | +28.8                               | +0.92          | -0.1                             | -0.1           |
| +30                     | +0.97        | +16.8                   | +0.50          | +16.6                       | +0.50          | +2.0                        | +0.06          | +19.3                               | +0.57          | -1.7                             | -0.06          |
| +20                     | +0.61        | +9.7                    | +0.29          | +13.6                       | +0.40          | +1.5                        | +0.05          | +13.0                               | +0.38          | -1.1                             | -0.03          |
| +10                     | +0.30        | +5.1                    | +0.15          | +4.9                        | +0.14          | +0.3                        | +0.01          | +5.1                                | +0.15          | -0.3                             | -0.01          |
| -10                     | -0.30        | -3.9                    | -0.12          | -10.2                       | -0.30          | -2.4                        | -0.07          | -11.1                               | -0.33          | -1.7                             | -0.05          |
| -20                     | -0.61        | -6.4                    | -0.18          | -13.4                       | -0.40          | -1.6                        | -0.05          | -15.9                               | -0.47          | -2.5                             | -0.07          |
| -30                     | -0.97        | -8.9                    | -0.26          | -17.5                       | -0.53          | -2.8                        | -0.08          | -19.7                               | -0.60          | -2.7                             | -0.08          |
| -40                     | -1.46        | -10.0                   | -0.30          | -21.2                       | -0.65          | -2.9                        | -0.08          |                                     |                | -3.7                             | -0.1           |

\* The declination of the images in the two eyes ( $\delta_b$ ) corresponding to the inclination of the beads when these appeared vertical is equal to cyclotorsion that has occurred (data for KNO).

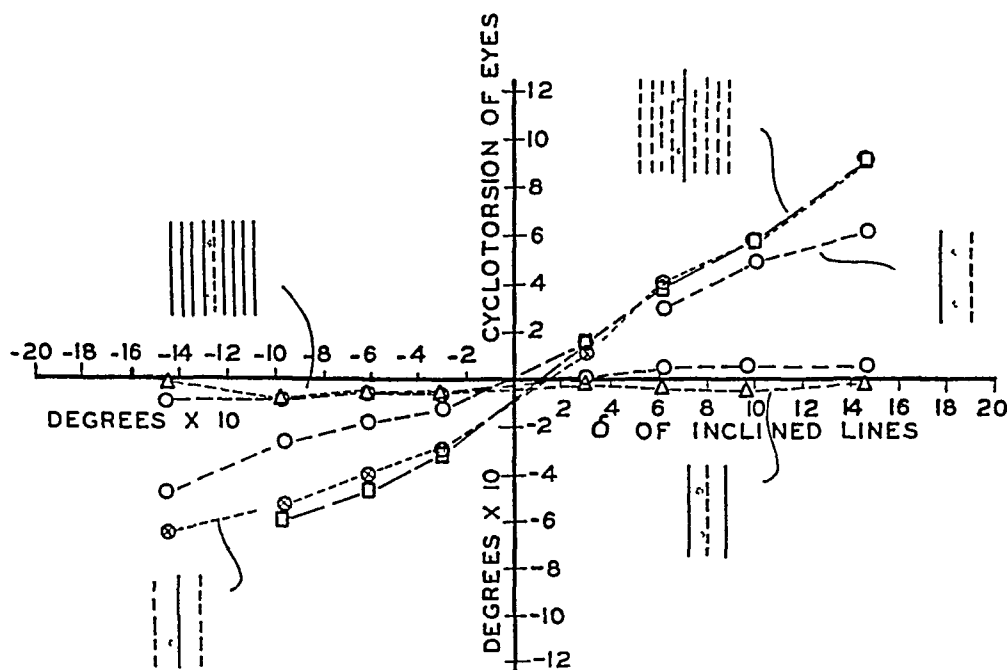


Fig. 13—Experiments which show that when a set of vertical contours and a set of inclined contours are present in the visual field, a cyclofusional movement occurs to compromise the resulting declinations of the images of the two sets. In the inserts, the solid lines indicate those contours that remain vertical, the dash lines, those that are inclined in space.

These experiments, in general, in which a series of parallel lines are inclined in space, are not wholly satisfactory because of perspective, which makes lines appear to converge at a distance, and this con-

vergence introduces a confusing empiric factor. There is no simple optical means without the use of other mirrors, which can be employed to overcome this situation. However, it appears that this factor has not seriously affected the results presented here.

Werner ascribed the phenomenon to "a change in the correspondence within the particular visual field." The nature of this "change in correspondence" is not clear, but in view of his other experiments reported in the same article a sensorial change is implied. Our experiments here make clear that there has been no change in the sensorial (or anatomic) correspondence between the retinas of the two eyes, but only a change in cyclotorsional positions of the eyes. This change might, however, be interpreted as a change of correspondence if that correspondence is related to external points in space the images of which fall on corresponding meridians.

#### COMMENT

The problem of cyclofusional amplitudes has been avoided in all the experiments described in this paper, partly because the optical-mechanical difficulties would be greatly increased if they were to be thoroughly investigated and also because these amplitudes are known to be so variable and so subject to training that the number of experiments would be interminable. Furthermore, there is a question whether any useful information beyond that found could be obtained from such data.

It would, of course, have been desirable to set up a suitable telescope, or similar device, to detect and to measure the actual cyclotorsional movements of the eyes in our experiments, as had been done by Brecher.<sup>13</sup> The magnitude of the movements here, however, is small, and when it is divided between the two eyes, the value for each is so small as to preclude practically such objective measurements. The precision to which Brecher could measure the cyclorotations was of the order of  $\frac{1}{2}$  to 1 degree, which, obviously, is not accurate enough here. To observe the linear movements of blood vessels near the limbus would also demand great precision, since a cyclorotation of the eye of 1 degree would give a displacement of only about 0.2 mm.

Under the controlled conditions described here, in which empiric factors and motives for depth perception are eliminated, in so far as possible, it is demonstrable that the eyes are capable of making cyclofusional movements of great precision. Thus, a standard deviation of  $\pm 0.07$  degree of declination was not unusual under optimal conditions. Such precision should be compared with stereoscopic thresholds of 5 seconds of arc, a precision which is significant in view of the small involuntary movements of the eyes (physiologic nystagmus) that are constantly present. In the case of stereoscopic thresholds, however,

these ocular movements may even aid the stereoscopic perception<sup>27</sup> In the experiments described here, the cyclofusional movements as measured through the stereoscopic perception of declinations between the images in the two eyes might not be so aided, except on the basis, which has been implied,<sup>28</sup> that these involuntary rotary movements always take place equally and in the same direction in the two eyes

Under our well controlled conditions, it has been shown that the eyes respond to stimuli from contours in either the horizontal or the vertical meridian and that even separated points of light, if disparate in the sense of declination, can provide sufficient stimuli for an actual cyclofusional movement The unsatisfactory responses previously found in the use of vertical lines can be attributed to their employment for determining cyclofusional amplitudes where doubling is the criterion

The results here show incontestably that the compulsion to cyclofusional movements arising from contours in the vertical or near vertical meridians is much greater than that from contours in other meridians, especially the horizontal This difference which is found between the vertical and other meridians is surprising and difficult to explain satisfactorily

However, the declinations between the images of vertical or near vertical contours also result in a stereoscopic perception of depth, while those of horizontal contours cannot That the processes of stereoscopic vision are rapid (of the order of several hundredths of a second, according to Langlands<sup>29</sup>) while the cyclofusional processes with horizontal contours are slow (of the order of one-half second, according to Verhoeff<sup>11d</sup>) may hold the key to the explanation Certainly, there exists a basis for suggesting that, in general, stereoscopic perception results from the compulsion to fuse disparate images, as Fleischer,<sup>30</sup> for example, has done In this sense, the processes of stereoscopic perception and those of the compulsion for fusional movements are interrelated and concomitant In that case, the cyclofusional movements compelled by the declinations of the images of vertical contours should be faster than those produced by the horizontal contours, and in being faster they accomplish the cyclotorsion before the compulsions from the horizontal contours can get under way

27 Marshall, W H, and Talbot, S A Recent Evidence for Neural Mechanisms in Vision Leading to a General Theory of Sensory Acuity, in Cattell, J Biological Symposia, Lancaster, Pa, Jaques Cattell Press, 1942, vol 7, pp 117-164

28 Duke-Elder, W S Text-Book of Ophthalmology, London, Henry Kimpton, 1932, vol 1, p 580

29 Langlands, N M S Experiments in Binocular Vision, Tr Optic Soc London 28 45-82, 1926

30 Fleischer, E Die Querdissparation als physiologische Grundlage des binokularen Tiefensehens, Ztschr f Psychol 147 65-132, 1939



The difference between the compulsions to fusion arising from vertical contours and those arising from horizontal contours cannot be associated with a sensorial difference in the perception of direction. It has been shown that lines can be set for the apparent vertical or horizontal meridians with considerable precisions, with no significant difference between the two<sup>31</sup>. However, this precision is much poorer for oblique contours<sup>32</sup>. The results described here show that the cyclofusional movements are roughly proportional to the declinations introduced. This would not be true when the declinations approach the limits of the cyclofusional amplitudes, where the amount of cyclofusional movement would be affected by cyclophorias and cyclotropias.

Clearly, the degree of cyclofusional movement varies not only with the configuration in the binocular field of view but with the contrast and relative weights of antagonistic declinations. This is to be expected on the basis of earlier investigations on the problem. Moreover, horizontal disparities between the images decrease the compulsion for cyclofusional movements. This may also be expected.

The results of these experiments explain satisfactorily the phenomenon of depth contrast of Werner. Likewise is explained the phenomenon in the space eikonometer, in which a meridional size lens at an oblique axis placed before the eye causes the oblique cross to appear inclined in space whereas the vertical plumb lines appear inclined only slightly or not at all, when according to geometric principles the reverse should be true.

In concluding this discussion, certain psychologic contrast effects should be mentioned. Hofmann and Bielschowsky<sup>33</sup> showed that a background of inclined contours affected one's conception of the meridian of the subjective vertical (not the stereoscopic vertical, but the vertical in the frontoparallel plane). The experiments of Vernon<sup>34</sup> and of Gibson<sup>35</sup> showed also that a prolonged observation of an inclined line (right or left) subsequently caused a vertical or horizontal line to appear inclined in the opposite direction. These effects are considered to be the result of experimental adaptive processes and are not concerned at all with the position of the eyes. However, all these observations should be considered in the light of the results of Noji<sup>16</sup>.

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31 Peirce, B. O. The Perception of Horizontal and of Vertical Lines, *Science* **10** 425-430, 1899.

32 Hofmann,<sup>17</sup> p. 599.

33 Hofmann, F. B., and Bielschowsky, A. Ueber die Einstellung der scheinbaren Horizontalen und Vertikalen bei Betrachtung eines von schrägen Konturen erfüllten Gesichtsfeldes, *Arch. f. d. ges. Physiol.* **126** 453-475, 1909.

34 Vernon, M. D. The Perception of Inclined Lines, *Brit. J. Psychol.* **25** 186-196, 1934.

35 Gibson, J. J. Adaptation, After-Effect and Contrast in the Perception of Tilted Lines, *J. Exper. Psychol.* **20** 553-569, 1937.

and Brecher,<sup>13</sup> which certainly suggest that cyclotorsions can, under certain conditions, follow the influence of external stimuli. The famous case of Sachs and Meller<sup>36</sup> is often cited to show that the subjective vertical can be adapted to new retinal meridians in the case of pronounced cyclotropia, possibly in the same sense that an anomalous "correspondence" can develop in a case of squint. None of these adaptive experiments has been performed for the stereoscopic vertical, though Gibson believes the same type of phenomena will be found there.

While these problems are outside the scope of this paper, the results would seem to imply that the retinal meridians which correspond to the subjective verticals are variable and subject to previous experience. The crux of this problem is whether the retinal meridians corresponding to the subjective stereoscopic vertical can be the same meridians as those of the monocular subjective vertical. Certainly, the experiments described in this paper, in which the visual plane of the observer is horizontal, suggest that the subjective stereoscopic vertical agrees accurately with the objective vertical. The angle  $V$  (of von Helmholtz, Volkman, and others) between the meridians of the apparent subjective verticals of the two eyes, if maintained in binocular vision, would make this result impossible. It is probable, however, that the measurements of this angle, like the majority of those dealing with torsions of the eyes with convergence and with elevation and depression of the eyes, are made with targets which permit the eyes to slide into a cyclophoric position.

The results of the experiments described here would provide evidence for the discussion of Hering's<sup>5</sup> theory concerning enforced cyclofusional movements, to the effect that the eyes can make adjustments which tend to keep the images of vertical contours in space on the retinal meridians for the stereoscopic subjective vertical, irrespective of the movements of the eyes. These cyclofusional movements probably occur, however, in any complex visual field where certain contours are inclined fore and aft with respect to the visual plane, in an effort to compromise the disparities in the interest of a single binocular vision.

#### STATISTICAL STUDY BASED ON SUBJECTS WITH ASTIGMATISM AT OBLIQUE AXES

Several studies<sup>37</sup> at the Dartmouth Eye Institute have made it possible to obtain data with the space eikonometer on nearly 400 subjects who had astigmatism at oblique axes.

<sup>36</sup> Sachs, M., and Meller, J. Ueber einige eigentümliche Lokalisationsphänomene in einem Falle von hochgradiger Netzhautinkongruenz, *Arch f Ophth* 57 1-23, 1904.

<sup>37</sup> Ogle<sup>10b</sup> Ogle and Madigan<sup>10c</sup> Burian and Ogle<sup>10d</sup>

It was pointed out that the correction of the astigmatism in these subjects would introduce meridional magnifications of the retinal images also at oblique axes and that associated with these magnification errors declinations of the retinal images of vertical (and horizontal) lines would exist. One could, if compensatory processes were not active, expect to find under controlled conditions an incorrect apparent inclination of vertical configurations. From the amount of this inclination it was hoped to find, by means of the space eikonometer, the magnitude of the declination error introduced by the corrected astigmatism.

In the space eikonometer, the test elements consisted of an oblique cross, a vertical line (or a central line configuration) through the center of this cross and two vertical plumb lines in front of and two behind the cross (cf fig 9 F). If a declination error were present, the central elements should not appear to lie in the plane of the cross. The experience of subjects with normal eyes was that with meridional size lenses placed before the eyes at oblique axes the cross appeared inclined. By means of the geared unit a suitable declination could be introduced to cause the plane of the cross and the center vertical elements to appear in the same plane, which usually also appeared substantially vertical. The same procedure of measurement was followed for the subjects with astigmatism at oblique axes.

The measured declination error,  $\delta_m$ , was shown<sup>19c</sup> to be correlated with the calculated declination error,  $\delta_o$ , computed on the basis of the amount and the axes of the astigmatic correction, the corneal astigmatism and the optical dimensions of the correcting lenses. This correlation was evidence of the stable organization of the retinal elements of the two eyes, according to the theories of Hering. It was shown, however, that on the average the measured declination error was less than the computed declination error by nearly one half.

This difference was explained on several hypothetical bases, one of which was the possible existence of cyclotropias. Until the present studies had been made, the nature of this possibility was not clear. Now inasmuch as the declination error associated with the aniseikonic errors at oblique axes would affect the images of the vertical elements but not those of the oblique cross, stimuli would be present for cyclofusional movements in the direction necessary to correct the declination between the images of the vertical lines. The cross would then appear inclined fore and aft in space. The declination introduced by the examiner using the geared unit to make the plane of the cross appear upright or to make the central vertical line appear to lie in the plane of the cross would measure the declination error as influenced by the degree of cyclotorsion present.

One would expect, however, that if the cyclofusional processes of the subject being tested were normal, as the correction for the true

declination error was introduced, the stimuli for the cyclofusional movement from the vertical elements would be reduced, so that in the end the true declination error would have been measured. However, if a residual cyclotopia remained, the true declination error could not be determined.

If one assumes that the calculated declination error,  $\delta_o$ , was the correct and true declination error, then, when the geared unit introduces a declination,  $\delta_m$ , to make the vertical element and the oblique cross appear in the same plane (that is, have the same inclination,  $\iota_c$ ) one can find, consequently, the theoretic cyclotorsion,  $\tau_t$ , from

$$\tan \iota_c = -\frac{b}{a} \tan \tau_t = \frac{b}{2a} (\tan \delta_o - \tan \tau_t - \tan \delta_m)$$

whence

$$\tau_t = \delta_m - \delta_o$$

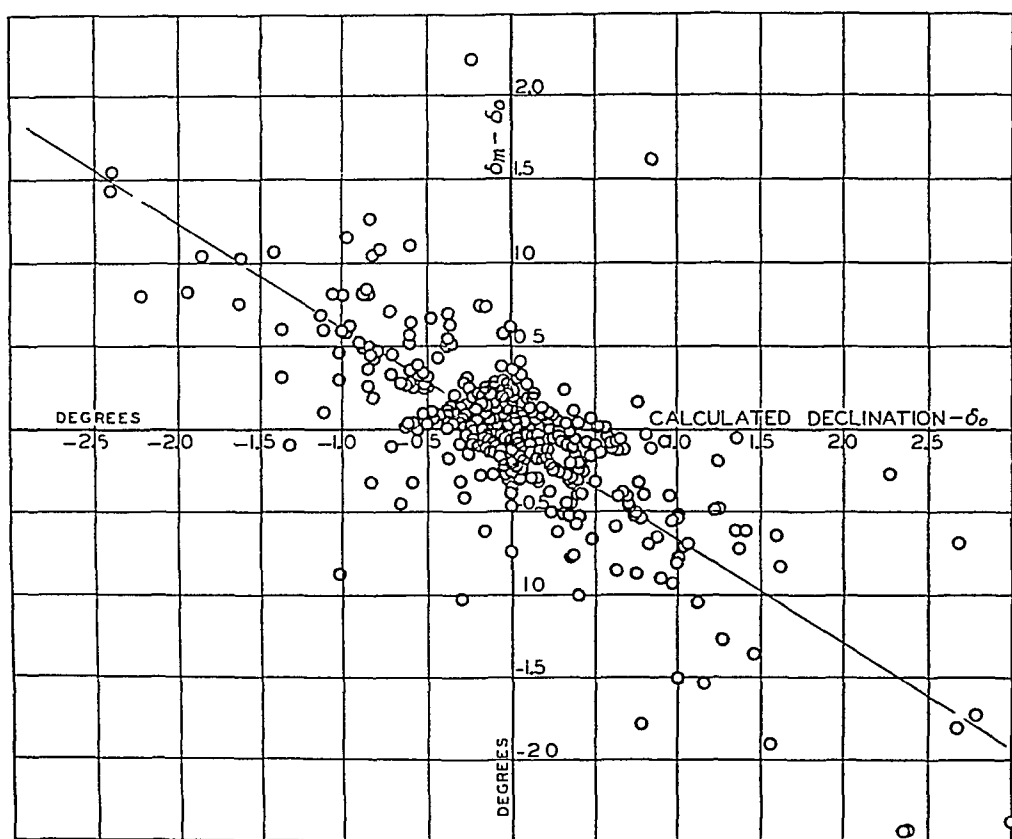


Fig. 14—Scatter diagram of the data from 400 subjects with astigmatism at oblique axes in which the differences between the measured and the computed declination errors,  $\delta_m - \delta_o$ , are plotted against the computed declination error,  $\delta_o$ . The difference ( $\delta_m - \delta_o$ ) is shown to indicate probably a disjunctive cyclotorsion of the eyes that exists at the time of measurement on the space eikonometer.

It was an easy matter, then, to calculate  $\tau_t$  with this formula from the data of the 400 cases.

According to the studies reported in this paper, the magnitude of the cyclofusional movement was roughly proportional to the declination introduced, hence, one might expect to find a correlation between the torsion,  $\tau_t$ , found and the declination error,  $\delta_o$ , calculated on the basis

of the corrected astigmatism. These values are shown in the scatter diagram in figure 14. Even a casual glance shows that a good correlation actually exists. A statistical analysis shows the Pearson coefficient of correlation to be 0.74, with a standard error of estimate of 0.36 degree, a value which certainly indicates significance. The degree to which these data show a lack of correlation may be due to other factors in the measurement of the aniseikonic error not connected with the correction of the astigmatic errors, but in spite of this the actual correlation found is significant. Further analysis of the data also shows that the distribution of  $\tau_t$  for the 400 cases is quite normal.

The only explanation of this correlation is that the majority of these subjects with astigmatism at oblique axes had small residual cyclotropias, which in direction tended toward the elimination of the vertical declination errors that had been introduced by the correction of the astigmatism. These cyclotropias must have been the result of the tonic innervations for those movements that had been constantly present during the time the subject wore the spectacles. To repeat, this study suggests that these subjects maintain cyclotorsional positions of the eyes in order partially to correct the declinations of the images of vertical contours that arise from the meridional magnifications accompanying the correction of the astigmatic errors.

The results of this discussion account for much of the discrepancy between the measured and the theoretic declination errors and add emphasis to the evidence of the previous paper<sup>10c</sup> that the physiologic organization of the two retinas is stable and must have been maintained independently of the origin of the astigmatism.

### SUMMARY

A review of the literature shows that there is now agreement that the external muscles of the eyes can, in the interest of maintaining binocular single vision, cooperate to provide cyclotorsions about the visual axes, which themselves may remain fixed. These movements have been designated as psycho-optical reflex movements.

In this paper are discussed experiments utilizing stereoscopic methods of spatial localization, which show that these cyclofusional movements occur much more freely than was heretofore realized. In the main these movements take place with any change in the type and orientation of configurations in the visual field. When the contours make up complex spatial arrangements that provide stimuli for cyclofusional movements of different amounts and in different directions, the movements that take place tend to compromise the antagonistic compulsions resulting from those contours. However, it is shown that contours whose images in the two eyes are vertical or nearly vertical provide much stronger stimuli for cyclofusional movements than do

those from contours whose images are horizontal. The explanation of this fact probably lies in the relative speeds of stereoscopic vision and of ocular movements. The importance of the results of these experiments to certain psychologic and physiologic concepts is discussed.

A statistical study of the data obtained from 400 subjects having astigmatism at oblique axes is presented. The results suggest that the eyes of these subjects maintain cyclotorsional positions that partially correct the declinations of the images which, in turn, arise from the meridional magnifications accompanying the correction of the astigmatic errors.

The correlation found emphasizes the stability of the organization between the retinal elements of the two eyes, discussed in an earlier paper.

Dartmouth Eye Institute

# Clinical Notes

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## PENICILLIN IN TREATMENT OF ACUTE ENDOPHTHALMITIS

### Report of a Case

S WEIZENBLATT, M D

ASHEVILLE, N C

**A**S DEEP extraocular infections of the eye often lead to loss of vision or of an eyeball, every new antibacterial agent has promptly been tried in treatment of such infections. Soon after the bacteriostatic action of penicillin and its additional favorable characteristics, such as absence of toxicity and easy solubility, were established, experimental work by von Sallmann<sup>1</sup> and Leopold<sup>2</sup> on rabbit eyes showed that systemic or iontophoretic application of this drug did not lead to any detectable concentration in the lens or vitreous. Topical application of penicillin gave high concentrations of this drug in the anterior structures of the eye<sup>3</sup> and was effective in treatment of infections of the anterior part of the eye due to penicillin-sensitive organisms, but only direct injection of this drug into the lens or vitreous<sup>4</sup> was of benefit in experimental infections of the deeper parts of the eye with certain strains of *Staphylococcus aureus*, and then only if given within twelve hours after the inoculation.

Publications on the bacteriostatic action of penicillin in deeper parts of the eye are not many, and the results are not uniform<sup>5</sup>. As the concentration of penicillin in the aqueous of experimental animals was found to be higher than that in the aqueous of the human eye, results obtained by intravitreal injection of penicillin in rabbit eyes which had been inoculated with *Staph aureus* or with pneumococcus need to be confirmed by further observation on the human eye. The following case may, therefore, be of interest.

1 von Sallmann, L. Penicillin and Sulfadiazine in the Treatment of Experimental Intraocular Infection with Pneumococcus, *Arch Ophth* **30** 426 (Oct) 1943  
von Sallmann, L, and Meyer, K. Penetration of Penicillin into the Eye, *ibid* **31** 1 (Jan) 1944

2 Leopold, I. H. Intravitreal Penetration of Penicillin and Penicillin Therapy of Infections of the Vitreous, *Arch Ophth* **33** 211 (March) 1945

3 Struble, G. J., and Bellows, J. G. Studies on the Distribution of Penicillin in the Eye, *J A M A* **125** 685 (July 8) 1944. Bellows, J. G. Penicillin Therapy in Ocular Infection, *Am J Ophth* **27** 1206 (Nov) 1944

4 Leopold<sup>2</sup> von Sallmann, L., Meyer, K., and Di Grandi, J. Experimental Study on Penicillin Treatment of Ectogenous Infections of Vitreous, *Arch Ophth* **32** 179 (Sept) 1944. Dunnington, J., and von Sallmann, L. Penicillin Therapy in Ophthalmology, *ibid* **32** 353 (Nov) 1944

5 von Sallmann, L. Penicillin Therapy of Infections of the Vitreous, *Arch Ophth* **33** 455 (June) 1945

## REPORT OF CASE

A white man aged 49 was admitted to the hospital on April 13, 1945, because of a painful infection in his only eye. The previous history revealed that Elliott's trephination with peripheral iridectomy had been performed on both eyes for chronic glaucoma in 1940. Six months later he lost the right eye because of a late infection with *Staph aureus*. Two infections occurred in the left eye in 1942, from which he recovered within four days. A third infection with *Staphylococcus albus*, in December 1943, resulted in purulent iritis, from which the eye recovered after oral treatment with sulfathiazole and injection of typhoid vaccine. Full vision was restored within four weeks.

*Present History*—April 13. The patient awoke with severe pain in his left eye and greatly impaired vision. Examination showed a high degree of edema of the lids, severe conjunctivitis and yellow infiltration of the bleb. The anterior chamber was cloudy and the iris extremely hyperemic, with a small, fixed pupil. The fundus was seen only indistinctly, the patient saw fingers at 3 feet (91 cm). Smear and culture revealed *Staph albus*. Treatment consisted in instillation of atropine, application of hot compresses, intravenous injection of typhoid vaccine, instillation of penicillin drops (2,500 units per cubic centimeter) every hour and administration of sulfadiazine, 80 grains (5.2 Gm) daily. Twelve hours later the pain in the eye had increased, and a hypopyon, measuring 2.5 mm, was present. Vision was limited to perception of hand movements before the eye. Penicillin, in 20,000 unit doses, was injected intramuscularly every four hours.

April 14. The condition of the eye was worse, the bleb was a solid plug of yellow infiltration, and the hypopyon was higher. The same treatment was continued, a second injection of typhoid vaccine resulted in a temperature of 105.6 F. The patient was confused and delirious.

April 15. The anterior chamber was clearer, the hypopyon smaller and the pupil well dilated, but a yellow reflex could be seen behind the lens in the temporal part of the vitreous. Projection was faulty. Two-tenths cubic centimeter of penicillin solution (2,500 units per cubic centimeter) was injected into the vitreous temporally and below after a preceding subconjunctival injection of procaine. Seven hours later the anterior part of the eye had cleared further.

April 16. About twenty-four hours after the intravitreal injection the cornea was steamy and hazy, the pupil dilated maximally and tension was plus 3. Use of atropine was discontinued.

April 17. The bleb was only slightly infiltrated, the cornea was clearer, the hypopyon was resorbed, and the iris was very hyperemic. Tension seemed normal. The vitreous was clearer.

April 18. Intramuscular injection of penicillin was discontinued. The patient's vision was improved.

April 20. The pain in the eye was worse. The cornea was hazy, with an irregular surface. The iris was less hyperemic. Tension was normal on palpation. A red reflex was obtained from the fundus. As the increased pain in the eye contrasted with the objective improvement of the endophthalmitis, the pathologic condition of the cornea was believed to be its cause and to be due to use of the penicillin drops, which was therefore discontinued.

The patient left the hospital fifteen days after the onset of the infection. At this time the eyeball showed a mixed injection, the bleb was very thin and transparent, the cornea and the anterior chamber were clear, the iris was hyperemic, and the pupil measured 6 mm (after instillation of atropine). Some exudate and pigment were present on the anterior capsule of the lens. The lens



was clear. In the vitreous were numerous floating opacities, and adjoining the retina, at the site of the injection of penicillin, was a large oval, perlucid opacity, with a convex membrane anteriorly. Vision was 20/70.

In another month vision was 20/20. The perlucid opacity in the vitreous had shrunk and become a white, glistening, oval structure, seemingly fixed near the retina. The patient had repeated ruptures of the bleb, with absence of the anterior chamber, and for this a plastic operation was performed on the conjunctiva in October 1945.

A check-up in February 1946 revealed a normal condition of the anterior part of the eye. The lens was clear, tension was 16 mm of mercury (original Schiøtz). The temporal half of the fundus showed many vitreous opacities, forming a network, which was visualized best with a +12 D lens, they converged to form a strandlike structure which continued toward the retina. No retinal atrophy was seen near the site of the injection of penicillin.

#### COMMENT

Local and systemic treatment with penicillin in the form of drops, combined with administration of a sulfonamide compound and fever therapy, checked the infection in the anterior part of the eye.

Deterioration of visual function continued, the intravitreal injection of penicillin stayed the abscess in the vitreous.

Considerable corneal irritation followed prolonged and frequent use of penicillin drops in high concentration (2 500 units).

An alarming, but temporary, increase in ocular tension was observed about twenty hours after the intravitreal injection of penicillin. Whether the latter complication arises only in eyes with glaucoma or in eyes which have been operated on for glaucoma, further observations will be necessary to determine. The increase of tension arose in an eye with a trephine opening in the corneoscleral junction.

A check-up ten months later revealed no visible damage to the retina or to adjoining structures at the site of the intravitreal injection.

Repeated infections of the bleb did not result in formation of scar tissue but led to thinning of its conjunctival covering, which ruptured spontaneously, with emptying of the anterior chamber.

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# Abstracts from Current Literature

EDITED BY DR WILLIAM ZENTMAYER

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## Anatomy and Embryology

COURSE OF THE PUPILLARY FIBERS IN THE OPTIC NERVE A BAKER,  
*Ophthalmologica* 104: 233, 1942

Cases are reported in which paralysis of the direct light reflex followed an injury to the optic nerve, whereas central visual acuity remained good. The optic disk showed atrophy. The consensual light reflex of the opposite eye was also abolished. The author believes that there are no facts known which make it necessary to assume the existence of separate pupillary and visual fibers.

F H ADLER

CIRCULATION OF BLOOD IN THE EYE F KISS, *Ophthalmologica* 106:  
225 (May-June) 1943

The eyes of newborn and adult human beings, rabbits, dogs and cats were given injections of india ink and then examined histologically. Some of the injections were made in the trunk of the ophthalmic artery and in the facial vein. The vascular system surrounding the canal of Schlemm was injected by introducing a needle with the material to be injected directly into the canal. The resorption of aqueous was determined by injecting the ink directly into the anterior chamber and killing the animals from six to twenty-four hours later. The preparations showed that the vasculature of the ciliary body consists of two parts (1) broad vessels of the ciliary process, and (2) narrow vessels confined to the region of the ciliary muscle. The first system is concerned with the production of aqueous, whereas the second forms the paths of resorption. It may be considered a second capillary region connected with the large veins of the iris. These veins, together with those from the canal of Schlemm, are bent here at a right angle or have a spiral course, so that when the intraocular pressure is increased the drainage in the veins may be impeded.

F H ADLER

## Bacteriology and Serology

A COMPARATIVE STUDY OF THE BACTERIOLOGIC FLORA OF NASAL AND NASOPHARYNGEAL MEMBRANES OF PATIENTS WITH CERTAIN OCULAR DISORDERS C BERENS and E L N CUMMING, *Am J Ophth* 28: 1313 (Dec) 1945

In a study of 277 sets of cultures of material from the nasal and nasopharyngeal membranes of 228 patients, Berens and Cumming found that in most instances cultures from both the nasal and the nasopharyngeal membrane are a far more reliable index of the presence of possible etiologic pathogens than are cultures from either site alone. Preliminary investigation suggests the necessity of securing cultures

from more than these two sites in order to obtain a satisfactory bacteriologic picture of the upper respiratory tract

W S REESE

### Conjunctiva

THE SULFONAMIDES IN OPHTHALMIA NEONATORUM A SORSBY and E L HOFFA, Brit M J 1 353 (March 11) 1944

An earlier report on 273 patients with ophthalmia neonatorum treated with sulfapyridine was published in the *British Medical Journal* (1:323, 1942) and abstracted in the *ARCHIVES* (28:342 [Aug.] 1942). In the present series the standard dose (a total of 2.5 to 4 Gm.) was used in an additional 258 cases. Sulfapyridine was employed in 133 cases, sulfathiazole, in 43 cases, sulfamezathine (dimethyl derivative of sulfadiazine), in 28 cases, and sulfadiazine, in 31 cases. In the remaining 23 cases more than one of these sulfonamide compounds was used, as there proved to be resistance or intolerance to the drug initially employed.

Of these 258 cases, clinical cure was obtained within eight days in 85.7 per cent, within three days in 29.9 per cent and in from four to eight days in 58.8 per cent, in 14.3 per cent the course was protracted. There was no appreciable difference in the action of the four sulfonamide drugs. Sulfapyridine, because of its greater toxicity, was the least desirable, and its use has been abandoned. Gonococcic infections responded more rapidly to sulfonamide therapy than did the nongonococcic infections. Inclusion bodies were found in 27 cases, in association with organisms in 2 cases and without such association in 25 cases. In these cases the infection responded well to sulfonamide therapy. Only exceptionally is a condition completely resistant to sulfonamide therapy. It is a matter of sluggish response rather than of total resistance.

ARNOLD KNAPP

### Cornea and Sclera

MEGALOCORNEA E ROSEN, Am J Ophth 28:1352 (Dec.) 1945

Rosen reports the case of a 26 year old soldier who showed bilateral megalocornea associated with embryotoxon, Krukenberg spindle, aqueous flare, iridodonesis and atrophic iris and dislocated lens. The author discusses megalocornea, taking issue with the statement that it is the "matter of a completely healthy eye in a healthy person." From a study of the literature it seems that megalocornea is not commonly associated with arachnodactyly, though the author has seen 1 case.

W S REESE

MODERN TATTOOING OF THE CORNEA C DJACOS, Arch d'opht 5:36 1945

The author points out that sympathetic ophthalmia has been a frequent complication of this procedure in the past and has been the cause of its falling into disrepute. In this paper he reviews Rollet's method of injecting india ink into a leukoma through a fine needle. The details of the procedure are described and 5 cases reported in detail. Djacos also describes the method of P. Knapp in which a solution of gold

chloride is used This is applied with a cotton swab after abrading the corneal surface He reports 2 cases, in 1 of which treatment was a failure He thinks that Rollet's method is much the better of the two and that it is much more easily controlled

S B MARLOW

NODULAR KERATITIS PRODUCED BY CATERPILLAR HAIRS G GARIBAY  
and A CORTES ZAVALA, *An argent de oftal* 5:136 (Oct-Dec)  
1944

A man aged 23 was awakened by a feeling of smarting in the lids of the right eye A caterpillar was found in the bed

Ophthalmic examination revealed edema of the upper lid, photophobia, lacrimation, conjunctival infection, a number of small corneal lesions, which stained, and iritis The corneal lesions resembled those of superficial punctate keratitis, but the severity of the ocular symptoms did not compare with those of that disease

Observation with the slit lamp showed that a series of white dots went deep into the corneal parenchyma, and in most of them a filament was present These were the hairs of the caterpillar Nodular formations, as observed by other authors, were not seen in the cornea or the conjunctiva

All the hairs were extracted, and the patient improved immediately The keratitis, or, rather, the ophthalmia produced by hairs of the caterpillar, as the author states it should be called, is caused by a poisonous substance which is secreted by glands located in the dorsal aspect of the worm and contained in the cential canaliculi of the hairs

H F CARRASQUILLO

### Experimental Pathology

RELATION OF ADRENAL GLANDS TO INTRAOCULAR PRESSURE M  
RADNOT, *Ophthalmologica* 108:137 (Sept) 1944

One adrenal gland was extirpated in a series of rabbits and the intraocular pressure measured with a Schiøtz tonometer for six days after operation The author states that the intraocular pressure is lowered on the side of the operation

F H ADLER

### General

TYPES, PAPER AND PRINTING IN RELATION TO EYESTRAIN R B  
FISHENDEN, *Brit J Ophth* 30:20 (Jan) 1946

In considering briefly some points of interest, several assumptions are made Illumination is on the basis of bright diffused daylight or artificial illumination, say, 20 foot candles The papers used are either white or lightly tinted, and the printing is done in black ink.

In the design of types there should be no serious departure from accustomed shapes Except for configuration, the major factor in type legibility is size Legibility depends on the size of the small, or lower case, letters Legibility will be reduced if the letters of the words are packed too closely, and it will be improved by inserting a space between the lines of type There are four types, all of good design, widely used. Baskerville, Fournier, Walbaum and Times

W. ZENTMAYER

PATHOGENESIS OF OCULAR COMPLICATIONS OF ARSPHENAMINE DERMATITIS S VON PASTINSZKY, *Acta dermat-venereol* 24 480 (March) 1944

Of 3 patients who had dermatitis with ocular complications as the result of antisyphilitic treatment with arsphenamine, the first had panophthalmitis, the second superficial keratitis punctata and the third corneal edema Von Pastinszky has observed that conjunctivitis is frequent in arsphenamine dermatitis with ocular involvement, but superficial keratitis is rare and corneal ulcers with perforation and panophthalmitis are still rarer This is due to the fact that allergic inflammations are not as likely to develop in the cornea as in the conjunctiva In addition to the allergic factor, secondary infection, lack of resistance, hypovitaminosis and perhaps mechanical factors may play a part The allergic nature of the inflammation is indicated by the extreme eosinophilia demonstrable in the conjunctival secretion

J A M A (W ZILTMAYER)

### General Diseases

THE OCULAR COMPLICATIONS OF LEPROSY J M DEBARROS, *Am J Ophth* 29 162 (Feb) 1946

DeBarros states that leprosy has a higher percentage of ocular involvement than any other systemic infection This involvement is restricted to the anterior segment, especially the cornea Iritis is found only in conjunction with corneal disease The author discusses the complication from an anatomic standpoint

W S REESE

MALARIAL PAPILLITIS R B LEWY, *War Med* 7 341 (June) 1945

Lewy examined a total of 60 patients for evidence of papillitis Some blurring and/or change in color of the optic disk was presented by 36, while the other 24 presented no change Ocular symptoms were usually mild Many of the patients said their eyes tired easily A number stated that they had blurring of their vision at about 50 yards (45 meters) Many of these patients had headaches, but this had to be discounted as this symptom was common to many patients with malaria who had no ocular changes Visual loss shown on the Snellen test chart was from 20/15 to 20/20 or 20/20 to 20/25 One patient lost vision to 20/100 in the right eye and 20/400 in the left It is recognized that the difference between papillitis and papilledema may be slight ophthalmoscopically It is also recognized that exudate or edema may be present in the neural or supporting tissue of the optic nerve as a product of either inflammation or stasis This condition is considered a papillitis because of the injected appearance of the nerve head in the majority of the patients and because many showed a disturbance in the ocular physiology, e g, diminution of visual acuity, reduced peripheral fields and enlarged blindspot scotomas No absolute correlation could be made between the amount of papillary change and the number of attacks of malaria The condition has been observed in patients with one attack and with eighteen The question may be raised whether medication is the cause None of the group of patients presented the retinal ischemia, arterial spasm and blindness characteristic of quinine amblyopia, which is often the cause of toxic retrobulbar

neuritis resulting in complete central blindness and pallor of the disk. One patient had a characteristic picture of the nerve head although he had never received quinacrine hydrochloride. The great increase in the use of quinacrine hydrochloride coincided with a drop in the incidence of malaria and papillitis. This should remove suspicion from quinacrine hydrochloride as a causative factor. There are many patients with papillitis who never received pamaquine naphthocate.

J A M A (W ZENTMAYER)

#### HISTOLOGIC CHANGES ASSOCIATED WITH RHEUMATIC INFECTION OF THE EYE J BABEL, *Ophthalmologica* 104: 243, 1942

The author reports a case of scleritenonitis occurring in a man aged 35 with endocarditis and myocarditis of rheumatic origin. The patient died, and a complete autopsy was performed, including the eyes. Death occurred while the scleritenonitis was in the process of recovery. The slides showed involvement of the sclera and Tenon's capsule as well as the ciliary body. The external ocular muscles also showed characteristic myocytes with nodules. Throughout the tissues there were perivascular infiltrates made up of plasma cells, lymphocytes and round, basophilic cells of histiocytic origin. The same histologic changes were seen in the myocardium, the endocardium and the synovial membranes.

F H ADLER

#### **Glaucoma**

#### NONPERFORATING CYCLODIATHERMY FOR THE TREATMENT OF GLAUCOMA F C LUTMAN, *Am J Ophth* 29: 180 (Feb) 1946

Lutman recommends cyclo-diathermy in hopeless cases for the relief of glaucomatous pain in preference to enucleation, retrobulbar injection of alcohol or roentgen irradiation. He states that it is particularly suitable in cases of glaucoma in which vascularization of the iris precludes operation on the iris or of glaucoma following venous thrombosis.

W S REESE

#### CATARACT AND CHRONIC GLAUCOMA C DUVERGER and P BREGEAT, *Arch d'ophth* 5: 3, 1945

Cataract and chronic glaucoma can develop in the same eye at the same time or one after another but without any relationship between them. Such a condition is sometimes difficult to diagnose. The surgical problem involved is first to protect the limbus above for a fistulizing operation and to operate on the cataract by an incision in the lower part of the limbus. If a membrane remains and the glaucoma still requires operation, the authors advocate doing a Lagrange sclerectomy above for operating on the membrane. Operation for glaucoma will be performed first even if the cataract is mature when the field of vision is restricted and the tension is above 30 or 40 mm. The cataract is removed later. In some of the cases in which the authors have performed operation the outcome has been very favorable. Sometimes the vitreous does not obstruct the fistula, which continues to function and the vitreous remains clear. As a rule the glaucoma is the chief cause of visual loss.

S B MARLOW

## Injuries

ORBITAL FOREIGN BODIES M L KRASNOV, *Vestnik oftal* 23: 10, 1944

A Navy school student aged 18 had been hit with a fist in the nose and the right orbit two weeks previously. There was loss of consciousness, accompanied with bleeding of the nose and vomiting.

The right upper lid was slightly edematous, and some roughness of the edge of the upper inner margin of the orbit could be detected on palpation. The media and fundus were normal. Visual acuity was normal.

The left eye presented total ophthalmoplegia, the pupil was dilated, with no reaction to light. The optic nerve was pale. The eye was blind. Roentgenograms showed nothing abnormal.

A few days later swelling of the skin of the right brow near the nasal side appeared, followed by some fluctuation. On incision a piece of pencil, 6 cm long, was found deep in the orbit. Two weeks later the ptosis of the left eye had nearly disappeared and the motion of the left eyeball was only slightly limited, but vision remained nil and the atrophy of the optic disk was complete.

The interest of this case lies in the fact that the presence of a large (6 cm) intraorbital foreign body was missed because of the history, the clinical picture and the normal roentgenogram, that such a large foreign body, in its oblique frontal entry and injury of both orbits, did not injure the eyeballs, and that there was no infection, so common in the presence of a wooden foreign body.

The roentgenogram taken after removal of the foreign body showed destruction of the bone about the left supraorbital fissure. It seemed that the piece of wood passed with force through the skin of the right brow and the medial wall of the right orbit, passed obliquely first through the right ethmoid bone and then through the left and finally lodged at the apex of the left orbit, injuring the bone in the supraorbital fissure and thus causing the total ophthalmoplegia.

O SITCHEVSKA

RESULTS OF THE USE OF SECONDARY SUTURES IN GRANULATING WOUNDS OF THE LIDS AND NEIGHBORING REGIONS P KOWALEWSKY, *Vestnik oftal* 23: 45, 1944

Observations in N Hospital showed that in 95 per cent of patients there was combined injury of the eyeball and the lids, the lids were partially or completely torn away and the bones of the orbit and the sinuses were injured. The multiplicity of injuries is characteristic of World War II, because of the intensity of trauma from fragments of mines, artillery shrapnel, aviation bombs and hand grenades.

The primary suturing of the lids and surrounding skin should be done carefully within six hours after injury in order to prevent large, deforming scars. However, about 60 per cent of patients with injuries of the eyes reached the hospital within four to eight days after the injury with granulations beginning to form. Secondary suturing of the wound at this stage by approximation of the lips of the wounds usually gave good union.

Late secondary suturing of injured lids is indicated (1) in injuries of lids in which the edges could be completely approximated, (2) in

extensive injuries of the lids and neighboring parts with restoration of the conjunctival sac, as well as in injuries of the inner and external canthi, and (3) for the reduction of size of the wound, the sutures to be applied only in places where the edges can be approximated

In infected wounds the secondary sutures are most favorable, placed on the eighth to the twelfth day after the injury. With injuries of the orbit removal of all fragments of bone is essential. The granulation tissue should be preserved, if necessary, double sutures can be used for the granulation tissue and for the skin. In the presence of deep pockets drains should be used. The bacteria found were the white staphylococcus, the diplococcus and the streptococcus, frequently a mixed infection was present. An ointment containing sulfanilamide in 10 per cent concentration and a sterile dressing gave a dry clean surface in two to three days.

Secondary sutures for the lids were used in 187 patients, in 81 per cent there was a smooth scar with primary union, in 11 per cent there was slight infection of the wound, and in 8 per cent the sutures had to be removed because of secondary infection.

Thus, Kowalewsky advocates the use of secondary sutures in injuries of the lids and adjacent parts, as, after careful preparation of the wound, they produce a smooth scar. This effect is important for cosmetic results and shortens the time of hospitalization.

O SITCHEVSKA

### Methods of Examination

#### A TRICK TEST TO DETECT NIGHT-BLINDNESS "MALINGERERS" E EPSTEIN AND S A HUGH LESSER, Brit M J 2: 644 (Nov 10) 1945

Tests of scotopic vision are all subjective and demand the cooperation of the patient. From a military point of view it is important to discover those who simulate night blindness, and the authors have devised the following procedure. They first attempt to show that the subject is cooperating fully. In that case any one of the various tests can be relied on. It is known that red light stimulates the cones of the retina only and that the rods are unaffected. This means that in subjects with normal central vision pure red light should be identified at minimal intensity even if the rest of the retina is diseased or defective. The minimum threshold for pure red falls within a narrow range of intensity of illumination. A subject with defective night vision but with normal cones should be able to see the red light within this narrow range of minimal intensity.

The method is as follows. After a careful routine examination, including tests for color vision, the subject is placed in a dark room and left to adapt to darkness for twenty minutes. After this time he is asked to state when he can just see the faint red light which is shown him and which is increased gradually in intensity. This test is repeated a number of times to determine whether the patient is cooperating or not. The malingerer reasons that he must not admit seeing the light until it is very bright, which, of course, does not correspond with normal macular function.



The apparatus used is Crooke's adaptometer 1944, which is fully described in the text with a diagram. The subject is at first tested without spectacles. It was found that many patients with high refractive errors gave subnormal results without their glasses and normal readings with them. Patients with small refractive errors usually gave the same result with or without glasses. A number of illustrative cases complete the article.

ARNOLD KNAPP

### Neurology

PHENOMENON OF VISUAL EXTINCTION IN HOMONYMOUS FIELDS AND PSYCHOLOGIC PRINCIPLES INVOLVED. M. B. BRUNDER and L. T. FURLOW, *Arch Neurol & Psychiat* 53:29 (Jan) 1945

The authors reviewed cases of syndromes due to cerebral injuries reported in the literature in which signs of "visual inattention in homonymous fields" or "hemianopsic weakness of attention" were noted. They studied a case of this type over a long period and found that the failure to appreciate an image on one side is not due to inattention but is the result of underlying normal psychologic mechanisms. They report this case in detail and discuss psychologic principles involved in a most interesting and instructive manner. In this case, in which a soldier had a gunshot wound of the left occipitoparietal cortex, various psychologic mechanisms became apparent during the advanced stages of restitution of visual function from right homonymous hemianopia. Visual stimuli originating in the normal homonymous field of vision tended to suppress or obscure the image originating simultaneously in the opposite, affected, field of vision. The more stimulation there was in the normal field, the less the patient saw in the pathologic field of vision. The affected field showed fluctuation of sensation. Rivalry, dominance and attention mechanisms are considered explanatory principles.

S. R. IRVINE

DENIAL OF BLINDNESS BY PATIENTS WITH CEREBRAL DISEASE. F. C. REDLICH and J. F. DORSEY, *Arch Neurol & Psychiat* 53:407 (June) 1945

The authors observed 6 cases of denial of blindness over a period of eighteen months in a 600 bed hospital. This fact demonstrates that the syndrome is not rare, but it is easily overlooked unless the examiner is aware of its existence. One is inclined to believe the statement of the patient who says he can see without an attempt at verification. Furthermore, most examiners are reluctant to make any attempt to stress forcibly to the patient such a severe defect as blindness. All patients who present such a syndrome are deteriorated and have disturbances of retention and orientation, hallucinations and delusions and neuropsychiatrists may look at their denial of blindness as one of many psychotic manifestations. Moreover, in most cases it is of little practical significance whether these blind patients affirm or deny their blindness, and the syndrome is therefore predominantly of theoretic interest.

The syndrome was caused by diabetic retinopathy in 1 patient, by atrophy of the optic nerve in another and by bilateral hemianopsia due

to tumor or to vascular lesions in 4 patients. Moreover, all patients had diffuse cerebral lesions. All showed intellectual deterioration, disorientation, severe impairment of recent memory and retention, and confabulation. The existence of bilateral focal lesions of the visual radiations or of the occipital visual areas leading to bilateral hemianopsia seems to play an important role in the pathogenesis of the syndrome. The interruptions of reverberating circuits between the thalamus and the sensory cortex constitute the outstanding etiologic factor.

S R IRVINE

OPTICOCIASMIC MENINGITIS. CLINICAL ASPECTS. PAUL GONZALEZ ENRIQUEZ, *An Soc mex de oto-rino-laring* 18: 17, 1943

The author gives a detailed discussion of the disease, illustrating it by means of a thoroughly studied case, with verification at operation and successful surgical treatment. He explains the varied symptomatology of the disease, taking into consideration the many anatomic structures in this location. Pathologically, he points out three varieties of the disease: the serous, the plastic and the cystic.

Twenty-seven per cent of cases of this condition occur between the ages of 20 and 30. As possible causes he mentions extension from the paranasal sinuses, syphilis, tuberculosis, infection with the colon bacillus, encephalitis, rheumatism and trauma.

The symptoms are local and general. General symptoms are headache, vertigo, vomiting and initial low grade fever. Local symptoms may be (1) optic, (2) hypophysial, infundibular or hypothalamic, or (3) frontal (disturbance of the first cranial nerve).

The ocular symptoms are most important. They include slight alteration of visual acuity (greater in cases of chiasmic involvement, in which atrophy frequently occurs), initial changes in the visual fields, with a temporal cut in the cases of chiasmic meningitis and concentric contraction in the cases of prechiasmatic involvement, and a central scotoma (in 31 per cent of cases). The appearance of the fundus is usually unchanged. The concentric contraction, before described as stellate, is the major ocular symptom.

The case presented is that of a schoolboy aged 17, whose chief complaints were intense cephalalgia and transitory states of amaurosis. He had other visual disturbances, vertigo, emotional and confusional states, polyuria, olfactory hallucinations and disturbances referable to the peripheral nerves.

The patient noted somnolence, increased weight (11 Kg), increase in output of urine and decrease in sexual desire. Physical examination showed nervous disturbances, weakness of the right side of the face, diminished tendon reflexes in the upper extremities and peculiar alterations in tactile and heat sensibilities in the upper part of the right arm.

Ophthalmologic examination showed initial bitemporal narrowing of the visual fields, which gradually progressed to concentric contraction. A bilateral annular scotoma was also found. The changes in the fundus were of no importance.

Roentgenographic and laboratory tests revealed no abnormality. With a diagnosis of opticochiasmic arachnoiditis, operation was performed. The clinical diagnosis was confirmed. The chiasm and optic

nerves were freed from adhesions. In four months the visual fields were normal, and the patient was free of symptoms.

The differential diagnosis is discussed in detail, the condition being differentiated from hysteria, epilepsy, lesion of the occipital lobe, encephalitis, meningitis, suprasellar tumor and migraine.

H F CARRASQUILLO

### Ocular Muscles

THE EFFECT OF OPERATIVE ALTERATIONS IN THE HEIGHT OF THE EXTERNAL RECTUS INSERTION J FOSTER and E C PEMBERTON, Brit J Ophth 30.88 (Feb) 1946

The authors have obtained the following effect from operative alteration of the height of the insertion of the external rectus muscle

|  | Prism Diopters |
|--|----------------|
| Whole width raising with resection and advancement | 11.2           |
| Whole width raising with resection alone           | 7              |
| Half width raising with resection and advancement  | 9              |
| Half width raising with resection alone            | 5.4            |
| Half width raising on the internal rectus muscle   | 2.75           |

From the results obtained from this procedure in 26 cases of concomitant squint, the authors conclude there is some justification for this operation when the vertical error is constant and less than 11 prism diopters at all horizontal angles. The eye moves in the direction in which the insertion is moved, and this movement is independent of the position of the conjunctiva.

W ZENTMAYER

### Operations

FULL THICKNESS SKIN GRAFTS FROM NECK FOR FUNCTION AND COLOR IN EYELID AND FACE REPAIRS J B BROWN and B CANNON, Ann Surg 121.639 (May) 1945

Brown and Cannon say that full thickness skin grafts from the neck and the clavicular region have been found to give superior results in the repair of facial defects. The amount of skin available is limited, but there is enough for the eyelids, for the nose and about the mouth. The color is nearly always close to that of the normal face. None of these grafts so far have had to have injection of pigment for color matching, whereas the dead whiteness or darkness of other grafts often leaves much to be desired. The second advantage is softness, and therefore better function. These grafts heal and have such thickness that the best kinesis of the grafted areas can develop. This property is best expressed in repairs of the eyelid, in which hard, boardlike scars of gasoline and phosphorus burns have been literally dug out of the lids and of the area from one eye to the other over the nose. When these areas are covered with the grafts from the neck, there are often dramatic relief of scar fixation and return to softness and function. The main areas for use of these grafts are on the lids, in the canthal regions, about the alae, over the nose and about the lips and angles of the mouth. As a rule, flap repairs are considered preferable for gunshot wounds, whereas grafts usually suffice for burns. However, about the lids, if a bed at all suitable can be obtained by dissection of the scars, these full

thickness grafts are used in preference to flaps and, it is thought, with better results. Donor sites can be closed, left open to granulate or grafted. They may make troublesome scars for a while, but no permanent serious trouble has been seen.

J A M A (W ZENTMAYER)

#### TWO STEP METHOD OF PLASTIC REPAIR OF THE CONJUNCTIVAL SAC B TOVBIN, *Vestnik oftal* 23:30, 1944

Excessive bleeding often interferes with the taking of conjunctival transplants. Tovbin therefore performs plastic operations on the conjunctiva in two steps. After having made the necessary incisions, a gauze tampon is packed into the conjunctival sac so as to produce the desired shape and is left there for three days, then the transplant is inserted. It usually takes well and does not shrink, and the prosthesis stays in well.

O SITCHEVSKA

#### Orbit, Eyeball and Accessory Sinuses

#### MALIGNANT EXOPHTHALMOS OR EXOPHTHALMIC OPHTHALMOPLÉGIA C ROBERTSON, *Australian & New Zealand J Surg* 14:262 (April) 1945.

Robertson reports 9 cases in which exophthalmos increased in spite of relief of the toxic symptoms. The suggestion that a different factor is at work in the production of malignant exophthalmos than is responsible for the exophthalmos of ordinary toxic diffuse goiter receives strong presumptive evidence when the age and sex grouping in the two conditions are compared. Toxic diffuse goiter is a disease of early adult life and is much more common in females than in males, while the malignant type of exophthalmos occurs in patients aged 40 or over and the sex incidence is almost reversed. Of the 9 patients, 6 were men and 3 women. In many cases the disease gradually dies out, but it often leaves the patient with an unsightly deformity and sometimes double vision. Only occasionally has complete regression of the exophthalmos occurred. In other cases the condition progresses until the disorganization of the eyeball is so great that excision of the globe has to be performed. It is now generally accepted that there is edema of all the orbital tissues outside the globe, and this increase in size of the orbital contents pushes the eyeball forward. It also restricts the free movements of the eyeball. It seems certain that the hormone responsible for the orbital edema is different from the one which produces the other signs of thyrotoxicosis. Since edema is a sign of water imbalance and since water balance is influenced by the pituitary gland, a pituitary hormone may be involved. Robertson treated 4 patients with Naffziger's method of decompression of the orbit, 1 had excision of the stellate ganglion, and 2 had high voltage roentgen therapy to the pituitary gland. None of these methods produced the desired results, some patients lost one or both eyes. Three patients whose metabolic rate was slightly minus after thyroidectomy were given thyroid when the eyelids became edematous and ophthalmoplegia appeared. The resulting increase in the metabolic rate increased the loss of body fluids, and the eyes receded. For 5 patients who did not receive surgical treatment therapy consisted in

raising the basal metabolic rate so as to increase water excretion. In all of them the disease was controlled.

J A M A (W ZENTMAYER)

### Uvea

IRIDOSCHISIS, WITH MULTIPLE RUPTURE OF STROMAL THREADS  
A LOEWENSTEIN and J FOSTER, Brit J Ophth 29.277 (June)  
1945

After a brief summary of previously reported cases characterized by local division of the stroma of the iris into two layers, the anterior of which floats in the aqueous, the authors summarize the clinical and histologic features of their own case.

In a woman aged 75 long-standing glaucoma changes in the iris consisted in a deep cleft between the anterior and the posterior layers of the stroma of the iris, parallel with the latter. The anterior layers were largely atrophic, and such tissue as remained was split into fibers, which were centered on a blood-containing vessel. These fibers were attached to the ciliary portion of the iris distally and were floating free in the aqueous.

The name iridoschisis for these changes is suggested.

The clinical and histologic observations suggest that the mechanism of these changes is the exaggeration of a physiologic aging process of the iris, in which the middle layers became atrophic. Subsequently the two layers are separated, and finally the threads of the anterior layer which remain and contain a blood vessel rupture and float free at one end.

The basic change is senile, but the process may be aggravated by proteolytic enzymes (lysins) in the aqueous, the product of glaucomatous metabolism.

The article is illustrated.

W ZENTMAYER

### Therapeutics

THE SUITABILITY OF EXPERIMENTAL CORNEAL LESIONS FOR EVALUATING LOCAL SULPHONAMIDE THERAPY. W T S COLE, J L HAMILTON-PATERSON AND ARNOLD SORSBY, Brit J Ophth 29 150 (March) 1945

Attempts to produce infective corneal lesions suitable for therapeutic tests in the rabbit with *Pneumococcus* types III and XIX by direct inoculation of the abraded cornea in the intact animal, by direct inoculation of the cornea after damage with solid silver nitrate and by direct inoculation exposure of the cornea by retracting the lids with sutures, all failed. Preliminary sensitization also failed to produce any satisfactory lesion on inoculation with the hemolytic streptococcus.

The method of intracorneal inoculation with *Pneumococcus* type XIX and *Staphylococcus aureus*, as described by Robson and Scott, did not appear to give lesions suitable for therapeutic tests.

In vitro experiments with *Bacillus pyocyaneus* to test the possibility that the conflicting results reported by Robson and Scott, on the one hand, and Klein and Sorsby, on the other, might be due to varying susceptibility of different strains of the organism to sulfanilamide gave negative results.

It is concluded that there is no valid experimental evidence that local use of sulfonamide compounds is effective in treatment of infections of the outer eye

W ZENTMAYER

MODERN ANTI-INFECTION TREATMENTS IN OPHTHALMOLOGY A  
MOREU, Arch Soc oftal hispano-am 4: 392 (May-June) 1944

Moreu treats the serious condition of seipiginous ulcer of the cornea as follows (1) A smear is made of material from the ulcer, (2) the lacrimal passages are explored, (3) if impermeable, these passages are treated immediately by means of dacryocystorhinostomy or dacryocystectomy, without wasting time in probing and irrigations, (4) atropine, 1 per cent, is instilled, (5) heat is applied, (6) 10 cc of milk is injected intramuscularly and (7) sulfamidotherapy (administration of sulfathiazole, up to 10 Gm in twenty-four hours) is instituted. All these steps are carried out within the first twenty-four hours after the patient is seen. If no improvement results, local treatment is begun at once. If there is improvement, one should wait forty-eight hours before instituting it. Local treatment consists in paracentesis of the anterior chamber at the limbus at 6 o'clock and letting out all the aqueous. Two cubic centimeters of blood is taken from the patient and 0.25 cc of this blood is injected into the anterior chamber, using a lacrimal cannula. The rest of the blood is put into a contact lens, which is placed over the cornea and kept there for two hours by means of a pad and adhesive tape. The author claims that this treatment cures the ulcer.

Purulent nidiocyclitis after cataract extraction was successfully treated as follows. Ten cubic centimeters of milk was injected, heat was applied, atropine and ethylmorphine hydrochloride were instilled, 20 tablets of sulfacetimide were administered in twenty-four hours, together with 3 tablets of nicotinic acid and 3 tablespoons of liver extract. The next day local treatment was instituted by injecting the patient's own blood into the anterior chamber. Another patient with a non-operative condition was treated in the same way. Both patients were cured and regained normal vision.

H F CARRASQUILLO

TREATMENT OF BURNS OF THE FACE WITH GRENZ RAYS M BALTIM,  
Vestnik oftal 23: 27, 1944

Baltin treated a number of burns of the face and lids of second degree with grenz rays. The effect of the treatment was noticeable in a few days, as the oozing stopped, the scales disappeared and epithelization began. One week of daily irradiation was sufficient to obtain good results.

O SITCHEVSKA

# Society Transactions

EDITED BY DR W L BENEDICT

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## ANNUAL CONGRESS OF THE OPHTHALMOLOGICAL SOCIETY OF THE UNITED KINGDOM

Charles B Goulden, M D, *President*

Frank W Law, M D, *Secretary*

J H Daggart, M D, *Reporter*

*May 30 and 31 and June 1, 1946*

Nearly 250 people, including some 50 visitors attended the annual congress of the Ophthalmological Society of the United Kingdom, held on May 30 and 31 and June 1, 1946, at the Royal Society of Medicine, 1 Wimpole Street, London, W 1, under the presidency of Charles B Goulden, O B E, M D, M Ch, F R C S. The success of this gathering was enhanced by the welcome presence of a number of distinguished foreign visitors, most of whom had been isolated in their own countries since 1939.

During his address of welcome to the guests and members, the president dwelt with satisfaction on the fact that many of the visitors from abroad were already old friends of British ophthalmologists. Special delight was expressed concerning the arrival of this year's Bowman lecturer, Dr Arnold Knapp, from the United States, and the president reminded his listeners that an invitation to deliver the Bowman lecture represented the highest compliment that could be paid by the society. He was confident, however, that Dr Knapp would maintain the tradition established by illustrious Bowman lecturers of former years. A cordial welcome was also extended by the president to Dr P Merigot de Treigny, the honorary secretary of the French Ophthalmological Society, to Prof H J M Weve and Dr E C Gravenmeyer, from the Netherlands, to Dr L Coppez, Dr L Bauwens, Madame Van Boven and Dr C L Schepens, from Belgium, to Prof B Semadini, Dr A Franceschetti and Madame Noelle Chome, from Switzerland, to Dr W H Melanowski, from Poland, to Dr H Gjessing, from Norway, to Dr Gunnar von Bahr, from Sweden, and to Dr Miguel Millan, from Chile. Before proceeding to deliver his presidential address, Mr Goulden referred hopefully to the prospect of an international congress being held in Europe in 1948.

The subject of the presidential address was Johannes Evangelista Purkinje, whose work, like that of many other eminent pioneers, was not recognized at its true merit until after his death. One obvious explanation for this neglect by his contemporaries was the fact that Purkinje's studies in clinical ophthalmology were written in ecclesiastical Latin. Moreover, he was often handicapped, especially in his earlier years, by lack of money and equipment. Mr Goulden reminded his

audience that Purkinje was born of poor Bohemian parents in 1787 and that he began to study for the priesthood at the age of 15 years. These studies, however, were abandoned at the age of 21, when Purkinje entered the School in Medicine in Prague. After a period spent as lecturer on anatomy at Prague, he moved to Breslau, where he achieved much notable work on microscopic anatomy, although at first he was denied the advantage of access to a proper microscope.

The president particularly stressed the versatility of Purkinje, whose work was by no means confined to ophthalmologic subjects. He made numerous discoveries in the realms of clinical medicine and pharmacology, as well as important contributions to the study of fingerprints. Among ophthalmologists his name is immortal, because the mirror reflections of a source of light by the cornea and by the anterior and posterior surfaces of the lens are known collectively as Purkinje's images. The name of Purkinje is also associated with a number of those entoptic phenomena which he studied with remarkable ingenuity.

A discussion on "Ocular Disturbances Associated with Malnutrition" was opened by Mr. Harold Ridley, who described the results of his army experiences among released prisoners in Rangoon, Singapore and other Far-Eastern centers. His address, which was packed with carefully assembled facts, was delivered at a high speed that prevented his listeners from appreciating all his lines of argument, but there is no doubt that study of the published paper will be interesting and informative to many of Mr. Ridley's colleagues. He frankly recognized the difficulty of deciding to what extent malnutrition was responsible for ocular lesions among people who were in many instances the victims of malaria, dysentery and other tropical maladies in addition to being underfed. He also admitted that it was impossible to define the exact stage at which relative pallor of the temporal side of the optic disk exceeded physiologic limits. One feature stressed by this speaker was the speed with which failure of central vision may develop in cases of riboflavin deficiency, so that the patient may suddenly become aware that he cannot distinguish the faces of his friends. In Mr. Ridley's experience the typical field defect was a scotoma involving the central 3 degrees. Constriction of the peripheral field was infrequent. Pallor of the optic disk, involving the temporal more than the nasal half, was the commonest ophthalmoscopic finding, but some patients displayed macular disturbance associated with obliterative changes in the arteries supplying the center of the fundus. Mention was made of partial recovery of vision in some cases, and the benefits of liver therapy were stressed. With regard to the somewhat controversial question of vascular arcades invading the periphery of the cornea, Mr. Ridley suggested that any lasting engorgement of the conjunctival vessels, whether due to riboflavin deficiency or not, can lead to this form of vascularization.

Air Commodore P. C. Livingston, the other speaker on this subject, was absent on Far-Eastern service, but Mr. Frank W. Law, the honorary secretary of the society, read extracts from his contribution. Air Commodore P. C. Livingston, assisted by a team of medical assistants and orthoptists, had observed a series of prisoners of the Royal Air Force returned from Japanese camps. Many of these victims had been compelled to perform heavy work on a diet containing less than one-third



the calories required for such activities. Among 3,000 men however only 200 (i.e., less than 7 per cent) suffered from visual defect. He pointed out that the prevalence of dysentery and other intestinal disorders often rendered the prisoners incapable of utilizing the whole of their inadequate diet, owing to its rapid passage through the bowel. The possible etiologic role of tobacco and wood alcohol in these cases of so-called nutritional amblyopia was discussed. According to An Commodore Livingston, other changes in the fundus besides partial atrophy of the optic nerve are by no means uncommon. Partial veiling of the retinal vessels by wisps of connective tissue was mentioned and he also spoke of impaired macular definition, of actual dots of degeneration or pigmentary stippling at the macula. Diagrams neatly constructed by Flight Officer Gwilt to illustrate central and peripheral field defects were shown. An Commodore Livingston also described the generous diet by means of which returning prisoners were built up, but he said that only a minority showed any recovery in visual acuity or diminution in the central scotoma.

When the subject was declared open for discussion most of the available time was occupied by those who had previously notified their intention of taking part. Mr T Keith Lyle, recently returned from overseas service with the Royal Air Force, gave a lucid account of his experience among prisoners from the Far East. He stated that he had seldom found any macular abnormality in these men, and he also stressed the lack of correspondence between the severity of the visual defect and the depth of pallor of the optic disk. One interesting feature, he said, was fragmentation of the central scotoma during the period of recovery. In discussing the question of vascular corneal loops near the limbus he mentioned that this phenomenon is exceedingly common in Calcutta, that the subjects also display angular conjunctivitis, glossitis and scrotal dermatitis and that all these lesions disappear when sufficient riboflavin is supplied in the diet.

Dr Hugh Stannus expressed his disbelief in the existence of a true retrobulbar neuritis due to beriberi and suggested that the part played by riboflavin deficiency in the causation of optic neuropathy was not fully settled. Having insisted on differentiating between toxic amblyopia and nutritional optic neuropathy, he went on to suggest that the latter may be combined with larger disturbances of the central nervous system and that dendrites are vulnerable to many varieties of defective diet.

Mr C D Shapland, recently demobilized from the Army Medical Service, reported that he had found evidence of a severe lesion of the optic nerve in 6 per cent of a series of 900 prisoners returned from Japanese camps. His paper contained numerous charts setting out the results of detailed medical and pathologic investigations on these patients. In the opinion of Mr Shapland, alcohol played no part in the production of visual defect in these prisoners, and tobacco during the period of captivity was so scarce that it could not be regarded as responsible for the lesions.

Among the subsequent speakers were several who had had the opportunity to examine prisoners released from Japanese camps. Prof H M J Weve, of Utrecht, Netherlands, pointed out that, although he had found many cases of central scotoma among prisoners returning from

Java, this disability was conspicuously absent in the victims released from German camps, even though the latter included many instances of starvation. Therefore, said Professor Weve, it must be assumed the existence of factors other than malnutrition, presumably some toxin peculiar to the Far East, is associated with dietary deficiency in the production of so-called nutritional amblyopia. Mr H M Traquair uttered a note of warning against the tendency on the part of some observers to assume that central scotoma necessarily indicates the presence of retrobulbar neuritis. Major Browning insisted that the condition known as beriberi is a clinical hotchpotch, that tropical medicine is in a state of flux and that his chief impression of ocular disturbances associated with malnutrition was their wide variability. Some patients complained of much pain, others had none. Retinal signs might be gross or lacking. The onset was rapid in some and slow in others. Major Browning's brief remarks helped to emphasize one inevitable conclusion to be drawn from the experiences of the various speakers, namely, that the subject is exceedingly complicated and that an immense amount of intelligently correlated research will be needed for its final solution.

Mr Harold Ridley, who received the president's warm congratulations on his contribution to the discussion, was given a chance to reply to some of the points raised by other speakers. He disagreed with Mr A H Lowther's suggestion that tobacco should be held partly responsible for the visual defects noted among returned prisoners, and he contended that deficiency of the B complex vitamins and restriction of the total protein intake were the main factors. Mr Ridley expressed the hope that these observations by numerous ophthalmologists on the consequences of Japanese prison diet might later be utilized to prevent ocular damage among the teeming multitude of Asia and India in times of famine.

The Bowman lecture, dedicated to the memory of William Bowman, the founder of the Ophthalmological Society of the United Kingdom, was delivered during the afternoon of May 30 by Dr Arnold Knapp, who delighted the audience with the fruits of his wide reading and rich experience. His subject, "The Present State of the Intracapsular Cataract Extraction," is one of absorbing interest to the great majority of ophthalmic surgeons, and Dr Knapp gave careful consideration to every aspect thereof. In the course of a historical survey, he referred in detail to the work of Smith, Barraquer, Elschnig, Sinclair, Mendoza, Verhoeff, Gradle, Arruga, Amsler and others. Special attention was devoted to the selection of cases and to the difficulties and complications likely to be encountered at operation. Every stage in the operative technic was exhaustively considered, with special emphasis on the importance of proceeding without undue haste during rupture of the zonular fibers. Dr Knapp reminded his listeners that senile thickening of the capsule is a change that usually develops concurrently with loosening of the attachment of these fibers. He went on to mention the advantages of akinesia and of retrobulbar injection. He also stated that he favored the superior rectus suture but was accustomed to leave it loose so that it could be used in an emergency. If the suture is tied down as a routine, the intraocular pressure is raised, and vitreous more readily escapes.

Dr Knapp stated that most of his patients underwent complete iridectomy, although he frankly recognized certain disadvantages in this step.

The question of corneoscleral suturing was carefully reviewed, and the lecturer pointed out that a properly applied suture not only diminishes the likelihood of prolapse of the iris and of hyphemia but also promotes early reformation of the anterior chamber. Dr Knapp expressed the firm belief that the patient whose anterior chamber does not promptly reform is exposed to the risk of secondary glaucoma. Other subjects considered were the choice of speculum, the incidence of loss of vitreous (5 per cent in Dr Knapp's later series of cases) and the occurrence of updrawn pupil, opacity of the anterior face of the vitreous and retinal detachment as sequels. The vital importance of a clean section was mentioned more than once. Dr Knapp admitted that the intracapsular method of cataract extraction is more difficult than the extracapsular, but he claimed that on the whole the intracapsular operation is safer and more efficient. At the end of the lecture, he was warmly congratulated by Sir Stewart Duke-Elder and by the president on his masterly survey, which will be closely studied by his listeners and by a host of other ophthalmologic friends all over the world when it appears in the forthcoming *Transactions* of the society.

At the end of the first day's session, the annual dinner of the society was held in the library and council room of the Royal College of Surgeons, Lincoln's Inn Fields. The foreign guests earlier mentioned by name attended the dinner, and the wives of many guests and members accompanied them. Among the guests were Lord Moran, president of the Royal College of Physicians, Sir Alfred Webb-Johnson, president of the Royal College of Surgeons, Mr Eardley Holland, president of the Royal College of Obstetricians and Gynaecologists, Mr P H Adams, president of the Ophthalmological Section of the Royal Society of Medicine, Mr H S Souttar, president of the British Medical Association, Air Marshal Andrew Grant, Director General of Medical Services, Royal Air Force, Mr Hugh F Powell, master of the Worshipful Society of Apothecaries of London, and Sir Wilson Jameson, chief medical officer to the Ministry of Health. The toast of the King, followed by that of the Queen, the Queen Mary, the Princess Elizabeth and the other members of the royal family, was proposed by Mr Charles B Goulden, the president of the Society. Sir Alfred Webb-Johnson, in proposing the toast of the society, made a graceful speech which revealed close familiarity with ophthalmologic interests. He recalled the links forged between ophthalmic surgery and the Royal College of Surgeons by William Bowman, the founder of the Ophthalmological Society of the United Kingdom, and he referred to the work of Cheselden. The president replied. To the toast of the guests, proposed by Sir John Parsons, Dr Arnold Knapp (the Bowman lecturer) and Air Marshal Andrew Grant replied. Finally, Sir Arnold Lawson, in proposing the toast of the president of the society, dwelt on Mr Goulden's quiet efficiency. The latter paid well deserved tribute to loyal and efficient help he had received from the honorary secretary, Mr Frank W Law. After the speeches had been completed, guests and members circulated for informal conversation, and many of them took the opportunity to gaze at the portraits of John Hunter, Lord Lister and other pioneers which adorn the walls of the council room at the Royal College of Surgeons.

On May 31, the second day of the congress, Dr A Lowenstein read a paper entitled "Perivasculitis Retinae of the Young (Eales's Disease)—a Pathologic Review" Sections of the eye and optic nerve of a man aged 21 were shown on the screen, and attention was directed to the presence of cellular infiltration of the retina Investigations, including animal injections made with a view to detecting the presence of tubercle bacilli, septic organisms and filter passers, all gave negative results The possible role of allergy in the production of this disease was discussed

Dr I C Michaelson's contribution, entitled "Traversing Intra-Ocular Foreign Bodies with Retinal Detachment," was also illustrated with numerous pictures He emphasized the differentiation of two main types (1) cases in which the flight of the foreign body is transvitreal and the ensuing detachment is attributable to immediate contusion or to bands of fibrous tissue developing in the vitreal after an interval, and (2) cases in which the flight is tangential In the latter variety, according to Dr Michaelson, a dense choroidal exudate is followed by contraction of white masses, visible ophthalmoscopically, and detachment can be seen to begin near the choroidal scar No detachment, on the other hand, occurs near the wound of exit of a transvitreal foreign body He advocated release of the subretinal fluid in cases of the second, or tangential, type of injury and insisted that no application of diathermy should be made in the neighborhood of the plastic choroiditis commonly present in such cases

"The Nerve Fiber Pattern of the Human Retina" was the title chosen for his paper by the president elect, Mr A J Ballantyne, who showed a number of diagrams to indicate the arrangement of nerve fibers spreading from the disk He stressed the existence of a small group of uncurved fibers passing direct from the optic disk to the macula Mr Ballantyne expressed the view that it is not yet known exactly how the upper and lower arching fibers interdigitate, and he also suggested that the macular syncytium has never been fully explained

Mr Eugene Wolff's contribution was entitled "The Mucocutaneous Junction of the Lid Margin" He sketched the routes followed by tears during their passage from the lacrimal gland to the puncta and emphasized the importance of blinking as a means of promoting their distribution In Mr Wolff's opinion, there is no need to invoke massage by the orbicularis as an explanation for the movement of tears Attention was specially directed to the precorneal film, which he described as consisting of three layers The layer in immediate contact with the cornea consists of mucus derived from the conjunctival goblet cells, and Mr Wolff suggested that these last-mentioned structures might appropriately be designated the "corneal polishing cloth" Next comes the intermediate layer, consisting of tears Most superficial of the three layers is a thin film of meibomian secretion, which not only acts as a kind of protective "flypaper" but also serves to prevent the middle layer of tears from running away too quickly or from being dissipated by rapid evaporation Furthermore, the meibomian secretion forms a low wall athwart the lower lid margin, thus enabling the conjunctival sac to function as a reservoir for tears For all these reasons, Mr

Wolff contended that the location of the mucocutaneous junction at the line of orifices of the meibomian glands must be recognized not merely as an academic fact but as a logical arrangement essential for the integrity of the cornea.

"Recent Developments in Artificial Eyes" were described by Mr E F Fincham who was introduced by the president. He reminded his audience that new plastic substances especially the acrylic resins, were already being introduced as substitutes for glass before the recent world war and that Mr Clarkson working at the East Grinstead Plastic Unit in 1941 was beginning to adopt the technic of mechanical dentistry with a view to improving the appearance of artificial eyes. A large proportion of Mr Fincham's paper was devoted to the problem of how to achieve close imitation of the iris structure. He contended that color and pattern must not be regarded as qualities isolated from each other.

Dr Mary Cripps described her experience in the "Treatment of Traumatic and Inflammatory Lesions by Roentgen Radiation and Short Wave Diathermy Combined." Her main conclusion was that these two methods of treatment reinforced each other, so that their beneficial effects were relatively disappointing when one was used apart from the other.

On the afternoon of May 31, 30 cases were presented at a clinical meeting held jointly with the Section of Ophthalmology of the Royal Society of Medicine. Among the patients were a number with war injuries and several prisoners returned from Japanese camps with partial atrophy of the optic nerve. In the absence of Mr P H Adams the president of the section the chair during discussion of the cases was taken by the senior vice president, Mr F A Williamson-Noble.

The official guests from abroad were entertained at dinner at the Hall of the Society of Apothecaries in the City of London on the evening of the second day of the congress by the council of the newly formed Faculty of Ophthalmologists. Mr Frank W Law the honorary secretary of the Faculty had fortunately been able by virtue of his connection with the Society of Apothecaries to secure permission for the dinner to be held in these agreeable surroundings where the guests were received by Sir Stewart Duke-Elder the president of the Faculty. After dinner short, informal speeches were made by Sir Stewart Duke-Elder, Miss Ida Mann, Sir John Parsons and all the guests from abroad, beginning with Dr Arnold Knapp. Unofficial views were exchanged with regard to the possibility of holding an international congress of ophthalmology in 1948.

On June 1, the third and last day of the congress, Dr D V Gini opened the program with a paper on the "Technic of Intracapsular Extraction of Cataracts with Retention of Conjunctival Bridge." He dwelt on the disadvantages of mutilating the iris, arguing that, even if it were true that iridectomy diminished the liability to prolapse—though he doubted that contention—any small advantage in that respect nevertheless was far outweighed by the dangers attending excision of a piece of iris. He also insisted as did Dr Arnold Knapp in the Bowman lecture, that depression of the globe increases the liability to loss of vitreous. Dr Gini also gave detailed consideration to pre-operative and postoperative treatment and his paper was followed by

an interesting discussion, during which Dr W H Melanowski, of Waisaw, spoke in support of the conjunctival bridge

Next came Dr W H Melanowski's paper on "The More Important Pages in the History of Ophthalmology in Poland" Having deplored the obscuration of Polish culture consequent on language difficulties and political upheavals down the centuries, Dr Melanowski proceeded to trace the advance of optical and ophthalmic knowledge in Poland from medieval times onward He referred to the life and work of Vitello, Novicampus, Sienius, Szokalski, Kamocki, Galezowski and Wicherikiewicz He reminded members of the society of the link forged by Johnstone between Poland and Scotland and recalled Zieminski's period of study at Moorfields Eye Hospital in 1888 Pictures of the famous Polish ophthalmologists were shown on the screen at the end of Dr Melanowski's talk and he then received the warm congratulations of Sir Stewart Duke-Elder

Dr C L Schepens, of Brussels, contributed a paper entitled "Is Malnutrition the Cause of Tobacco Amblyopia?" He began by saying that tobacco amblyopia was rare in Belgium and Holland before the recent world war but that its incidence was greatly increased during the German occupation In Dr Schepens' opinion, this increased incidence was partly due to the inferior quality of the tobacco in general use During the preparation of high grade tobacco a large proportion of nicotine undergoes oxidation, but this substance is abundant in "green" tobacco, especially in the home-grown kinds Inferior tobacco did not, however, entirely account for the prevalence of tobacco amblyopia during the war years, for even those who were smoking stores of prewar tobacco displayed an increased susceptibility to the malady Malnutrition from shortage of protein, fat and vitamins was clearly the other main factor, and in this connection it is worthy of note that the victims all complained of other symptoms besides the visual defect

Indigestion was invariably present Cramps, deafness and other disturbances were by no means uncommon Other features of wartime tobacco amblyopia noted by Dr Schepens were a lowered average age of incidence, a lower average consumption of tobacco and a higher proportion of changes in the fundus, especially in the younger age groups He showed numerous charts displaying scotomas near the center of the field but emphasized that the characteristic early change in the fields is a pericecal disturbance His experience led him to believe that tobacco amblyopia is essentially due to lower capacity of the liver to neutralize toxins and that it is a disease of the retina rather than of the optic nerve, although of course the nerve will undergo consecutive degeneration when the retinal changes have reached an irreversible stage

Dr Schepens was warmly congratulated by Mr H M Traquair, who went on to stress the importance of high blood pressure as an etiologic factor in tobacco amblyopia Mr Traquair also pointed out that in a predisposed subject an attack of tobacco amblyopia could be precipitated by a fracture, a sharp cold or various other physical disturbances, and even by the onset of mental worry Dr H Gjessing remarked that tobacco amblyopia was common in Norway during the war of 1914 to 1918 when fats were scarce Sir Stewart Duke-Elder

emphasized the relationship between Dr Schepens' observations and the experiences reported by the speakers in the discussion on "Ocular Disturbances Associated with Malnutrition" Having commented on the variety of toxins and dietetic defects which might combine to degrade the metabolism of the central nervous system, Sir Stewart expressed the hope that many of the clinical conditions that now seem to be distant may with advancing knowledge be shown to possess a common denominator

- Mr T W Letchworth's paper on "Stereoscopic Vision in Binocular Aphakia" was autobiographic He recently underwent a successful operation, by Mr O G Morgan, on the left eye for extraction of cataract Vision in the right eye, the lens of which is opaque is 6/12 with the aid of a small correction, while the left eye obtains 6/6 vision with a correction of  $+6.0$  D sph  $\subset +4.0$  D cyl, axis 160 Mr Letchworth emphasized the distortion inevitably produced by the peripheral portion of a strong spectacle lens but claimed that he can readily fuse his right and left images so long as he is looking through the axial portion of his left glass For work that demands visual precision he uses a contact glass over the left eye but finds it easy to drive a motor car while wearing his ordinary spectacles

Mr A Seymour Philips' paper on "Venous Changes in the Retina in Diabetes" was illustrated by excellent fundus pictures drawn by the author himself He referred to the propensity of retinal veins in a diabetic subject to split into numerous small twigs, which coalesce farther on Sacculation, entailed by sudden changes in caliber, was another characteristic feature, and in some instances veins that had undergone prolonged dilatation might be converted into fibrous tissue Mr Philips suggested that whereas thrombosis occurs as a result of rapid venous obstruction, slowly progressive obstruction of the veins might offer a reasonable explanation for the changes observed with diabetes He showed a similar fundus picture of advanced retinal phlebosclerosis in a young man with advanced pulmonary fibrosis and posed the question whether the venous changes in the retina characteristic of diabetes may be due to increased and variable blood pressure Insulin, of course, entails violent fluctuation in the level of blood pressure Mr Philips admitted that his argument was somewhat weakened by the absence of similar venous changes in the fundi of victims of glaucoma, but Mr Affleck Greeves, in the course of the subsequent discussion, mentioned that he had often observed venous changes in cases of long-standing glaucoma and suggested that thrombosis of the central retinal vein, occurring as a complication of glaucoma and indicative of sudden complete venous blockage, is often preceded by slowly advancing partial obstruction in the retinal veins Mr A J Ballantyne, whose paper dealing with this subject in the society's *Transactions* for 1943, page 101, had been mentioned by Mr Philips, attributed the changes to a combination of venous stasis and disease of the vessel walls He stressed the slow development of diabetic retinopathy, as shown by cases in which punctate hemorrhages may precede exudates by several years When once the internal limiting membrane has been transgressed, however, rapid changes supervene, leading to retinitis proliferans Dr I C Michaelson drew attention

to atonia of the capillary system as a factor promoting congestion of the retinal veins in such conditions as diabetes and leukemia

At next year's congress, Mr A J Ballantyne, the new president of the Ophthalmological Society of the United Kingdom, will be assisted by the normal number of two honorary secretaries, Mr James Doggart and Mr E F King. Thus, Mr Frank Law will be relieved of the honorary secretaryship which he has held single handed for the last six congresses. In spite of difficult wartime conditions, there has been no break in the continuity. Although the *Luftwaffe* made a London meeting inadvisable in the spring of 1941, Mr Law was able to arrange for the congress to be held in Cambridge during September of that year. Then from 1942 onward London was the place of assembly. Mr Law's untiring efforts were crowned by the success of this, the 1946, congress, which was due in such large measure to his efficient organization.



# News and Notes

EDITED BY DR W L BENEDICT

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## GENERAL NEWS

**Army Institute of Pathology and American Registry of Pathology**—What is now known as the Army Institute of Pathology was established in 1863 as the Army Medical Museum. During World War II the activities of the Institute were greatly expanded, especially in the field of diagnostic pathology and research. There are now on file over 170,000 accessions. The results of research at the Institute during the past few years will be published in a volume of about fourteen hundred pages as a part of the official history of World War II. The present director is Col J Ash, who will be succeeded on October 1 by Col Raymond O Dart.

On request of Major General Norman T Kirk, the Surgeon General of the Army, the Committee on Pathology of the National Research Council, Division of Medical Sciences, in late 1945 prepared a report on the future development of the Institute. The report has been approved by the Surgeon General and by the War Department.

The essential recommendations in this report are (1) that a new building of adequate size be constructed, (2) that the Institute be organized in four divisions—Department of Pathology, Army Medical Illustration Service, Army Medical Museum and American Registry of Pathology—each headed by a competent specialist, (3) that the staff of the Institute be drawn from both the commissioned ranks of the Army and from the civilian professions, (4) that a comprehensive educational and training program be undertaken, (5) that the vast store of material at the Institute be used for research, and (6) that the services in pathology in the Veterans Hospitals be centralized at the Institute.

The American Registry of Pathology, founded in 1922, thus is and will continue to be, an integral part of the Army Institute of Pathology. There were, on Jan 1, 1946, over 43,000 cases registered. To effectuate the new plans as they relate to the Registry, the National Research Council, Division of Medical Sciences appointed a Committee on the American Registry of Pathology. The members of the Committee are Howard T Karsner, chairman, Cleveland, Col J E Ash, Washington, D C, Brig Gen R Callender, Washington, D C, Col Baldwin Lucke, Philadelphia, Robert A Moore, St Louis, Benjamin Rones, Washington, D C, A R Shands Jr, Wilmington Del, and Henry A Swanson, Washington, D C.

At the present time there are fourteen registries as a part of the American Registry of Pathology. These include Registry of Ophthalmic Pathology, established in 1922, sponsored by the American Academy of Ophthalmology and Oto-Laryngology, Lymphatic Tumor Registry, established in 1925, sponsored by the American Association of Pathol-

ogists and Bacteriologists, Bladder Tumor Registry, established in 1927, Kidney Tumor Registry, established in 1940, and Prostatic Tumor Registry, established in 1943, sponsored by the American Urological Association, Registry of Dental and Oral Pathology, established in 1933, sponsored by the American Dental Association, Registry of Otolaryngological Pathology, established in 1935, sponsored by the American Academy of Ophthalmology and Oto-Laryngology, General Tumor Registry, established in 1937, sponsored by the American Society of Clinical Pathologists, Registry of Dermal Pathology, established in 1938, sponsored by the American Academy of Dermatology and Syphilology, Chest Tumor Registry, established in 1942, sponsored by the American Society for Thoracic Surgery, Registry of Neuropathology, established in 1943, sponsored by the American Association of Neuropathologists, Registry of Orthopaedic Pathology, established in 1943, sponsored by the American Academy of Orthopaedic Surgeons, Registry of Veterinary Pathology, established in 1944, sponsored by the American Veterinary Medical Association, and Registry of Gerontology, established in 1945, sponsored by the Gerontological Society, Inc

Plans for additional registries are under consideration. A professional scientific society wishing to sponsor a registry should communicate with the Director, Army Institute of Pathology, Seventh Street and Independence Avenue, S W, Washington 25, D C. The society appoints a committee to work with the Director in supervision of the activities of the Registry, and make an annual contribution to the budget, which is administered by the National Academy of Sciences.

All specimens in the Registry are available for review and research by competent investigators. Sets of slides and accompanying syllabuses on special fields are available for loan to the civilian professions and officers in the federal services. Physicians, dentists and veterinarians are urged to send unusual specimens together with an abstract of the history to the Registry. The contributor receives a report on each specimen and is asked to keep the Registry informed of the follow-up on the patient.

With the reorganization of the Army Institute of Pathology to be completed during 1946 and 1947, a full time scientific director of the American Registry of Pathology will be appointed, and sufficient clerks and technicians will be available to assure adequate use of the registries for diagnosis, research, training of young men and education of the professions.

**American Registry of Pathology**—Many diseases are so rare that any one individual, or even the staff of any one hospital or clinic, has a limited opportunity to study certain conditions and lesions. Conclusions in science must be based on not one but many observations. Therefore, it is desirable to organize and support central agencies for the collection and filing of histories, specimens and follow-up studies.

For over twenty-four years the American Registry of Pathology has been maintained at the Army Institute of Pathology in Washington, D C. It was founded in 1922 by the then curator of the Army Medical Museum, Brig Gen George R Callender, at the request of the American Academy of Ophthalmology and Oto-Laryngology. Succeeding curators

Major Paul E McNabb, Col Virgil H Cornell, Col Raymond O Dait and Col J Earle Ash, have given time and thought to the problems of the Registry. On Jan 1, 1946, material from over 43,000 cases was on file.

There are now fourteen separate registries, each sponsored by a professional scientific society. Important additions to knowledge have been made by investigations at the Registry, notably on tumors and diseases of the eye, tumors of the lymphatic system and tumors of the bladder.

With the reorganization of the Army Institute of Pathology and with plans for the erection of a new building, sponsored by Major General Norman T Kirk, the Surgeon General, the American Registry of Pathology takes on increased importance. There will be greater opportunities for the training of specialists, for research and for educational activities.

The American Registry of Pathology deserves support from the civilian professions in terms of contributions of materials by individuals and sponsorship of registries by societies.

**Oftalmologicheskiiy zhurnal**—A new monthly journal of ophthalmology is being published in the Soviet Union. Heretofore *Vestnik oftalmologii* was the only journal in that country devoted to ophthalmology. In their foreword, the editors (V Filatov, S Kalfa and V Arkhangelsky) state that the journal will be devoted to problems of prevention of blindness. Reconstructive plastic surgery, keratoplasty, and the pathogenesis, diagnosis and treatment of glaucoma and trachoma are some of the other subjects on which leading articles will be published. Space will be devoted to the ophthalmologists from the provinces for the publication of their clinical and theoretic work. A consultation column will be established for them.

The first issue contains the following articles: "Biogenic Stimulators", "Elastometric Curves in Glaucoma", "Penicillin in Treatment of Thrombosis of the Cavernous Sinus", "Tissue Therapy in Contusion Chorioretinitis", "Tissue Therapy in Ocular Diseases of Hypertensive Origin", "Electromagnets in Ophthalmic Practice" and "The Fundus in Wounds of the Skull."

The price is 8 rubles.

**The Scientific Exhibit, Atlantic City Session of the American Medical Association**—At the Atlantic City Session, June 9 to 13, 1947, the American Medical Association will observe its centennial anniversary. For almost half of those hundred years—since 1899—the Scientific Exhibit has been a feature of each annual session and has developed into a short course in graduate medical instruction.

Exhibits at the 1947 Session will cover all phases of medicine. A certain amount of historical material will be included but emphasis will be placed on the latest developments of medical science. The Committee on Exhibits of the Section on Ophthalmology consists of Dr Georgiana D Theobald, Chairman, 715 Lake Street, Oak Park, Ill., Dr Derrick Vail, Chicago, and Dr A B Reese, New York.

Applications for space should be submitted as early as possible, since the closing date is Jan 13, 1947. Application blanks may be obtained either from the Committee members or from the Director, Scientific Exhibit, American Medical Association, 535 North Dearborn Street, Chicago 10

**Proctor Lecture in Ophthalmology.**—The University of California announces the receipt of \$20,000, given by Mrs Francis I Proctor for the establishment of a lecture in memory of her husband, the late Dr Francis I Proctor. The first lecture will be given by Dr Kenneth Swan, professor of ophthalmology at the University of Oregon Medical School, who will speak on "Contemporary Concepts of Pharmacology and Toxicology of the Cornea." The lecture will be given in Toland Hall of the University of California Medical School in San Francisco on Friday, December 20. This lectureship will be a yearly one.

**Research Study Club of Los Angeles**—The sixteenth annual mid-winter post-graduate clinical convention in ophthalmology and otolaryngology, sponsored by the Research Study Club of Los Angeles, will be held Jan 20 to Jan 31, 1947. The first week will be devoted to the eye.

The following teachers will take part: Dr William L Benedict, Dr Henry P Wagener, Dr Kenneth C Swan, Dr David O Harrington, Dr Dohrmann K Pischel and Dr Meyer Wiener. The fee for the clinical course is \$75. Applications should be sent to Dr Pierre Viole, 1930 Wilshire Boulevard, Los Angeles 5. Owing to the difficulties of obtaining accommodations, it is well to write at once for reservations to Mr H M Nickerson, manager, Elks Club, Douglas MacArthur Park, Los Angeles 5.

**The George Washington University Department of Ophthalmology.**—The seventh annual W Thornwall Davis Intensive Post-graduate Course in Ophthalmology will be given the week of Feb 3 to 8, 1947, at the George Washington University School of Medicine, 1335 H Street, N W, Washington, D C, by the resident staff and the following guest lecturers: Dr F Heed Adler, Philadelphia, Dr J Mason Baird, Atlanta, Ga, Dr S Judd Beach, Portland, Maine, Dr Hermann M Burian, Boston, Dr Ramon Castroviejo, New York, Dr C Alvin Clapp, Baltimore, Dr F Bruce Fraclick, Ann Arbor, Mich, Dr Deane B Judd, Washington, D C, Dr Peter C Kronfeld, Chicago, Dr Walter I Lillie, Philadelphia, Dr Angus L MacLean, Baltimore, Mr Philip L Salvatori, New York, Dr Harold G Scheie, Philadelphia, Dr Edmund B Spaeth, Philadelphia, and Dr Frederick W Stock, Durham, N C.

The tenth annual W Thornwall Davis Post Graduate Course in Ocular Pathology, and Orthoptics and Surgery will be given during the week of Jan 27 to Feb 1, 1947. This is a practical course and is limited to 30 registrants.

The secretary, May Everist Kramer, Suite 34 1801 K Street N W, Washington 6, D C, will be glad to furnish on request further details regarding the post-graduate courses in ophthalmology.

**Howe Lecture in Ophthalmology**—Prof William John Brownlow Riddell, fellow of the Royal Faculty of Physicians and Surgeons, and dean of medicine at Glasgow University gave the Howe lecture in Ophthalmology on "Heredity and Variation in Clinical Ophthalmology" at the Harvard Medical School on Tuesday, Nov 19, 1946

#### SOCIETY NEWS

**Washington, D C, Ophthalmological Society**—The first meeting of the Washington, D C, Ophthalmological Society for the 1946-1947 season was held on Monday, Nov 4, 1946, and was a joint session with the Baltimore Ophthalmological Society

Dr Richard W Wilkinson, president of the Washington, D C, Ophthalmological Society, presided at the meeting Case presentations of cataracta neuromodermatica and vitreous cyst were made by Dr Edward J Cummings Dr Jules B Chapman presented a case of cataracta complicata

The guest speaker of the evening was Prof W J B Riddell, of the University of Glasgow Scotland His presentation was on the "Clinical Valuation of Cataract Operation," and the discussers of this interesting paper were Dr Clyde A Clapp, of Baltimore and Dr John W Burke, of Washington, D C

A short business meeting followed this discussion, and the meeting was then adjourned until the next session, scheduled for Jan 6, 1947

**Belgian Society of Ophthalmology**—The Belgian Society of Ophthalmology celebrated its fiftieth anniversary by a meeting in Brussels on Sept 28 to 30, 1946 The meeting was opened on Saturday September 28, at 3 p m, in the presence of Her Majesty, Queen Elisabeth, in the marble hall of the Palais des Academies The presidential address was given by Professor van der Straeten A message of the foreign delegations was delivered by Professor van der Hoeve, Dr Leon Coppez spoke on the scientific work of the society since its foundation, and "The Human Eye in Art" was the subject of an address by Dr Alaeys

On Sunday September 29, the Belgian Society of Ophthalmology met in the Maison des Medecins, 54 boulevard de Waterloo, at 10 o'clock in the morning, with Professor Weekers presiding The following papers were read "Blindness of the Newborn," Prof J Beauvieux, delegate of the French Society of Ophthalmology, "Ophthalmology in the War Years," Dr Law, delegate of the Ophthalmological Society of the United Kingdom, "Certain Lesions of the Ciliary Arteries," Professor Zeeman, delegate of the Netherland Society of Ophthalmology, "The Aqueous Humor, That Unknown Quantity," Professor Ansler, delegate of the Swiss Society of Ophthalmology

At 3 o'clock in the afternoon, with Professor van Canneyt in the chair, the following papers were presented "Ocular War Injuries from 1939 to 1944," J Sedan and G Farnasier (Marseille), "Sympathetic Ophthalmia Cured by Subconjunctival Injections of a Sulfonamide Compound Report of Three Cases," G Renaud (Paris), "The Oily Precorneal Layer," E Wolff (London), "The Technic of Transplantation of Corneal Grafts," G P Soumille (Nantes), "The Vasodilator

Action of Nicotinic Acid on the Blood Vessels of the Retina" (an experimental and clinical article), Henrique Moutinho (Lisbon), "Hypertensive Retinopathy and Hypophysial Diabetes," R Onfray, Derot and Quentin (Paris), "Retinitis of Septic Origin, Report of Two Cases," R Lindsay-Rea (London), "Proliferating Retinitis and Cleavage of the Retina," S Schiff-Wertheimer (Paris), "A Spontaneously Curable Form of Macular Retinal Exudation, Probably Tuberculous," G Renard (Paris), "A Short Account of Orthoptic Training," M Pugh (London)

On Monday, September 30, there was an excursion to Antwerp, with a visit to the Rubens house and to the Cathedral, with breakfast at the "Century," in de Keyser Avenue, and in the afternoon a drive was taken in the city, with a visit to the tunnel under the Escaut

#### PERSONAL NEWS

**Research Project on Onchocerciasis Completed**—Dr William B Clark, head of the department of ophthalmology, Tulane University of Louisiana School of Medicine, returned to Guatemala on Nov 7, 1946, where he concluded the research project on onchocerciasis which he began there last year. He returned to New Orleans on Nov 16, 1946

## Book Reviews

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Fourteenth Report of the Memorial Ophthalmic Laboratory, Giza, Cairo, 1939-1944 Ministry of Public Health Price, 35 piasters Pp 140 Cairo, Egypt Schindler's Press, 1945

This report covers the period of the war years from 1939 to 1944 and consists of a selection of the more important papers of scientific interest prepared during that time. Owing to excessive costs, all illustrations have been omitted. Reference is made to seventeen other papers by members of the staff, not included in the report but all appearing in issues of the *Bulletin of the Ophthalmological Society of Egypt*. Case reports of special clinical and pathologic interest, which were a prominent feature of previous (annual) reports of this laboratory, are also omitted.

Twelve papers are given. The first, by the director, Rowland P. Wilson, is entitled, "Trachoma. A Selection of Personal Observations and Experiences." It reports the author's observations on the disease over an eighteen year period. Under the heading of etiology are comments on the early studies on Bacterium (*Noguchia*) granulosis and the reasons which led to its elimination as an etiologic possibility. The author then mentions the steps which led him to conclude that trachoma is a virus disease, in which the inclusion bodies of Halberstadter and Prowazek are the intracellular colonies of the virus. Under the head of epidemiology he notes that in Egypt trachoma is pandemic, affecting as high as 100 per cent of village populations. He notes that many factors, in particular the acute ophthalmias, are concerned in the spread of the disease but that the observance of simple personal hygienic principles would be sufficient to prevent its spread in most cases. Wilson does not believe that there is any special racial susceptibility, although he notes that the tendency to spontaneous cure is more evident among Egyptians than among Europeans. He then describes his observations in cases of incipient trachoma and stresses the fact that the virus infects the limbal epithelium at the same time that it infects the palpebral conjunctiva. He concludes with observations on the pathologic character of follicles, on differential diagnosis, on prophylaxis and on sulfonamide therapy.

In a second paper, Wilson discusses the economic importance of the acute ophthalmias and makes recommendations for their control. He includes statistics on the incidence of the ophthalmias in the various age groups and their effect on visual acuity. It is estimated that at least 75 per cent of the blindness in Egypt is produced by the acute ophthalmias, with approximately 120,000 Egyptians blind in both eyes from this cause. Wilson believes that there is every reason to hope that sulfonamide therapy alone can prevent entirely the serious sequelae of these diseases, as well as reduce indirectly the incidence of trachoma.

In a third paper, Wilson and Bland present bacteriologic and clinical observations on treatment of the acute ophthalmias with the sulfonamide

compounds and with penicillin. They conclude that the sulfonamide drugs are of much greater value than penicillin, particularly in the treatment of Koch-Weeks conjunctivitis.

This paper is followed by one by Bland on spontaneous folliculosis of the conjunctiva in grivet and vervet monkeys, with observations on the susceptibility of the grivet to the trachoma virus. Bland concludes that the reaction of grivets and vervets to trachoma cannot be distinguished histologically or clinically from spontaneous folliculosis and that these animals are therefore unsuitable for research on trachoma. He notes, however, that the trachoma virus still produced trachoma in a human volunteer after four passages in the grivet, inclusion bodies, present in the original inoculum, could not be found in the grivet but reappeared in the case of experimentally produced human trachoma.

In an important article, entitled "The Etiology of Trachoma: A Critical Review of Present Knowledge," Bland concludes that the trachoma virus bears a close relationship to the viruses of inclusion conjunctivitis, lymphogranuloma venereum and psittacosis. He further concludes that these viruses stand in an intermediate position between the rickettsias and the large viruses. He prefers to call them "basophilic viruses," on account of the blue staining of their initial bodies.

The volume concludes with five short reports by other members of the laboratory staff. El-Tobgy describes a scheme for massive abortive treatment of the acute ophthalmias with chemotherapy and recommends sulfapyridine, sulfadiazine or sulfathiazole, given in a daily dose of 0.5 Gm for each 20 Kg of body weight over a four day period. Kamel reports on schistosomiasis (bilharziasis) of the conjunctiva and notes that up to 1936 only 3 cases of the ocular disease had been seen in the laboratory. Since then, however, he has seen an additional 5 cases. He notes that the lesions are not painful and that the patient's attention is attracted to them only by reason of the disfigurement they cause. Kamel reports on clinical and histopathologic observations in 3 cases of leishmaniasis involving the eyelids. He notes that roentgen therapy and diathermy have been most efficacious. Nashed reports on chemotherapy of the acute ophthalmias and concludes that oral treatment is more successful than local application. Along similar lines, Hilmi Hamed describes results of experiments in the treatment of Koch-Weeks and gonococcal conjunctivitis and sulfapyridine. He recommends a combination of intramuscular injections and oral therapy.

The director notes that the scientific work of the laboratory was in large part interrupted by the war. The twelve papers included in the fourteenth report, however, contain much of value, and the more significant ones will be abstracted separately.

PHILLIPS THYGESON

Studies from the George Washington University School of Medicine,  
1943-1944. Washington, D. C., 1944.

Among the forty-eight reprints there are two on the eye. "Military Ophthalmology," by W. T. Davis, and "Leiomyoma of the Iris," by W. T. Davis, E. Sheppard and W. J. Romejko. Both these articles were published in the *American Journal of Ophthalmology* and have been reviewed.

ARNOLD KNAPP



**Clinical Ophthalmoscopy** By Arthur J. Bedell, M.D., F.A.C.S., D.Sc., LL.D. Two hundred glass-mounted Kodachrome 2 by 2 inch reproductions with concise history and description of each. Price, \$100. James A. Glenn, 76 Columbia St., Albany N. Y. 1946.

Since the publication of Jaeger's "Atlas," in 1855, the illustration of lesions of the fundus has engaged the attention of many ophthalmologists. In England, Frost's "Atlas" appeared in 1896, and there were many beautiful illustrations in the *Transactions of the Ophthalmological Society of the United Kingdom* which were also the work of that eminent artist, A. W. Head. Oeller's "Atlas," in 1896, was the first atlas in which the reproductions were made in oils, and they were painted by the author. A beautiful atlas in color was published by di Marzio in 1937, in Italy.

The era of fundus photography was initiated with Dimmer's painting work, which began in 1905 and was summarized in an atlas by Dimmer and Pillat in 1927, but photographic reproduction did not come into its own until the Zeiss works brought out the Nordenson camera based on modern optical principles (Gullstrand), with which excellent photographs were taken and the procedure came into general use. Tille et Couadau's "Atlas" appeared in France in 1939, and Bedell published his "Atlas on Fundus Photographs" in 1939. Photographs in color could not be taken on account of the necessarily long exposure, but with the manufacture of the more sensitive films of the present day this difficulty was surmounted and splendid photographs in color are now in general use. Dr. Bedell is a pioneer in photography of the fundus, and his beautiful pictures in colors have illustrated many papers and enlivened many medical meetings. He has now brought out the first kodachrome atlas of fundus pictures. In a series of 200 glass-mounted Kodachrome, 2 by 2 inch (5 by 5 cm.) reproductions, the subject of ophthalmoscopy is systematically covered. A small accompanying manual brings a concise history and gives a description of each picture. The series begin with the normal fundus and its congenital anomalies, then come circulatory disturbances associated with hypertension and arteriosclerosis, lesions of the blood vessels, diabetes, senile macular degeneration, retinochoroiditis, tumors of the choroid, angiomas of the retinae, retinitis pigmentosa, angiod streaks, changes of the optic nerve, glaucoma, traumatic lesions and intraocular foreign bodies. The color, the details and the depth perception are as true to life as the image with the ophthalmoscope at its best. The much sought after colored photographic reproduction has finally been obtained, and Dr. Bedell can be proud of his success in the difficult mastery of the intricate subject of fundus color photography. These pictures are by far the best that have been published and it is a pleasure to study them and to enjoy their beauty. At last a collection of transparencies has been made available for teaching ophthalmoscopy, and the student can now see and study the fundus picture without reflexes in all its true and beautiful colors.

This collection of kodachromes comes in two secure metal boxes and at a very reasonable price, there are empty places for 100 additional slides, which it is to be hoped that Dr. Bedell will gradually fill with additional beautiful photographs in the years to come.

# Directory of Ophthalmologic Societies \*

## INTERNATIONAL

### INTERNATIONAL ASSOCIATION FOR PREVENTION OF BLINDNESS

President Dr P Baillart, 66 Boulevard Saint-Michel, Paris, 6<sup>e</sup>, France  
Secretary-General Prof M Van Duyse, Université de Gand, Gand, Prov Ost-flandern, Belgium  
All correspondence should be addressed to the Secretariat, 66 Boulevard Saint-Michel, Paris, 6<sup>e</sup>, France

### INTERNATIONAL OPHTHALMOLOGIC CONGRESS

President Prof Nordenson, Serafimerlasarettet, Stockholm, Sweden  
Secretary Dr Ehlers, Jerbanenegade 41, Copenhagen, Denmark

### INTERNATIONAL ORGANIZATION AGAINST TRACHOMA

President Dr A F MacCallan, 17 Horseferry Rd, London, England

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President Dr Harry S Gradle, 58 E Washington St, Chicago  
Executive Secretaries Dr Conrad Berens, 35 E 70th St, New York Dr M E Alvaro, 1511 Rua Consolacão, São Paulo, Brazil  
Place Habana, Cuba Time February 1948

## FOREIGN

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Secretary Dr Frederick Ridley, 12 Wimpole St, London, W 1

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Secretary Dr D S Shen, Eye, Ear, Nose and Throat Hospital, Chengtu, Szechuan, China  
Place Eye, Ear, Nose and Throat Hospital, Chengtu, Szechuan, China

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Secretary Dr F S Tsang, 221 Foochow Rd, Shanghai

### CHINESE OPHTHALMOLOGICAL SOCIETY OF PEIPING

President Dr H T Pi, Peiping Union Medical College, Peiping  
Secretary Dr C K Lin, 180 Hsi-Lo-yen Chienmeng, Peiping  
Place Peiping Union Medical College, Peiping Time Last Friday of each month

\* Secretaries of societies are requested to furnish the information necessary to make this list complete and keep it up to date

## FACULTY OF OPHTHALMOLOGISTS

President Brig Sir Stewart Duke-Elder, 63 Harley St, London, W 1, England  
 Secretary Mr Frank W Law, 45 Lincoln's Inn Fields, London, W C 2, England

## GERMAN OPHTHALMOLOGICAL SOCIETY

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 Secretary Prof E Engelking, Heidelberg

## HUNGARIAN OPHTHALMOLOGICAL SOCIETY

President Prof I Imre, Budapest  
 Assistant Secretary Dr Stephen de Grosz, University Eye Hospital, Mariautca 39, Budapest  
 All correspondence should be addressed to the Assistant Secretary

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President Dr W Niccol, 4 College Green, Gloucester, England  
 Secretary Mr T Harrison Butler, 61 Newhall St, Birmingham 3, England.  
 Place Birmingham and Midland Eye Hospital

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 Secretary Mr William M Muirhead, 70 Upper Hanover St, Sheffield 3  
 Place Manchester, Leeds, Newcastle-upon-Tyne, Liverpool, Sheffield and Bradford,  
 in rotation Time October to May

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 Secretary Dr Mohammed Khalil, 4 Baehler St, Cairo  
 All correspondence should be addressed to the secretary, Dr Mohammed Khalil.

## OPHTHALMOLOGICAL SOCIETY OF HOSPITAL DE NUESTRA SEÑORA DE LA LUZ

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President Dr D D Sathaye, 127 Girgaum Rd, Bombay 4, India  
 Secretary Dr H D Dastur, Dadar, Bombay 14, India  
 Place H B A Free Ophthalmic Hospital, Parel, Bombay 12 Time First  
 Friday of every month

OXFORD OPHTHALMOLOGICAL CONGRESS

Master Mr F A Williamson-Noble, 27 Harley St, London, W 1, England  
 Secretary-Treasurer Dr F A Anderson, 12 St. John's Hill, Shrewsbury, England.  
 Place Oxford Time July 3-5, 1947

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 Secretary Dr J Sobanski, Lindley'a 4, Warsaw  
 Place Lindley'a 4, Warsaw

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President Dr José T Pico, Avenida Ponce de Leon 15, San Juan 10  
 Secretary Dr Ricardo F Fernandez, Avenida Ponce de Leon 15, San Juan 10.

REVISTA BRASILEIRA DE OFTALMOLOGIA

President Dr Caldas Britto, Largo de Carioca 5-6° andar, Rio de Janeiro, Brazil  
 Secretary Dr Evaldo Campos, R Rodrigo Silva 7-1° andar, Rio de Janeiro, Brazil  
 Place Rio de Janeiro, Brazil Time Third Friday of every month from April  
 to December

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 Secretary Dr Harold Ridley, 60 Queen Anne St, London, W 1, England

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 Place Edinburgh and Glasgow, in rotation

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 Secretary Dr Oscar F Horstmann, Calle 5ta #702, Vedado, Habana, Cuba  
 Time Second Tuesday of every month

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 Secretary Dr Arturo Etchemendigaray, Villa Constitución, Santa Fé  
 Place Rosario Time Last Saturday of every month, April to November All  
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Secretary Dr Jorge Luis Castillo, Mendoza 421, Tucumán, Argentina

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Place Atlantic City Time June 9-13, 1947

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 Place 91 Lincoln Park South, Newark Time 8 45 p m, second Monday of  
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 Place Honolulu Time Third Thursday of each month

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President Dr Howard F Hill, 177 Main St, Waterville, Maine  
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 Place Massachusetts Eye and Ear Infirmary, 243 Charles St, Boston Time  
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AND OTOLARYNGOLOGY

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 Place Miami, Florida Time Nov 6, 1946

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 Place University Club, Denver Time 7 30 p m, third Saturday of each month, October to May, inclusive

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 Place French Lick Time First Wednesday in April

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 Secretary Dr Gabriel Tucker, 250 S 18th St, Philadelphia 3

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 AND OTOLARYNGOLOGY

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 Secretary Dr William A Kennedy, 372 St Peter St, St Paul 2  
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 Secretary Dr Fritz D Hurd, 309 Medical Arts Bldg, Great Falls

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 Secretary Dr. Thomas H Johnson, 30 W 59th St, New York

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 Secretary-Treasurer Dr C W Kuhn, 1020 S W Taylor St, Portland 5  
 Place Good Samaritan Hospital, Portland Time Third Tuesday of each month

## PENNSYLVANIA ACADEMY OF OPHTHALMOLOGY AND OTOLARYNGOLOGY

President Dr Thomas F Furlong Jr, 36 Parking Plaza, Ardmore  
 Secretary Dr Benjamin F Souders, 143 N 6th St, Reading  
 Time Last week in April

## RHODE ISLAND OPHTHALMOLOGICAL AND OTOLOGICAL SOCIETY

Acting President Dr N Darrell Harvey, 112 Waterman St, Providence  
 Secretary-Treasurer Dr Linley C. Happ, 124 Waterman St, Providence  
 Place Rhode Island Medical Society, Library, Providence Time 8 30 p m,  
 second Thursday in October, December, February and April

## SOUTH CAROLINA SOCIETY OF OPHTHALMOLOGY AND OTOLARYNGOLOGY

President Dr J H Stokes, 125 W Cheves St, Florence  
 Secretary-Treasurer Dr Roderick Macdonald, 330 E Main St, Rock Hill

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 Place University Club, Salt Lake City Time 7 00 p m, third Monday of  
 each month

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 Secretary-Treasurer Dr V C Malloy, 2d National Bank Bldg, Akron, Ohio  
 Time First Monday in January, March, May and November

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President Dr B M Cline, 153 Peachtree St N E, Atlanta, Ga  
 Secretary Dr Lester A Brown, 815 Doctors Bldg, Atlanta, Ga  
 Place Academy of Medicine Time 7 30 p m, fourth Monday of each month  
 from October to May

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Chairman Dr Jonas Friedenwald, 1212 Eutaw Pl, Baltimore  
 Secretary Dr Fred Reese, 330 N Charles St, Baltimore 1  
 Place Medical and Chirurgical Faculty, 1211 Cathedral St Time 8 30 p m,  
 fourth Thursday of each month from October to March

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 Secretary Dr W Chunn Parsons, 425 Woodward Bldg, Birmingham, Ala  
 Place Tutwiler Hotel Time 6 30 p m, second Tuesday of each month, Sep-  
 tember to May, inclusive

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President Dr Benjamin C Rosenthal, 140 New York Ave, Brooklyn  
 Secretary-Treasurer Dr Louis Freimark, 256 Rochester Ave, Brooklyn 13  
 Place Kings County Medical Society Bldg, 1313 Bedford Ave Time Third  
 Thursday in February, April, May, October and December

BUFFALO OPHTHALMOLOGIC CLUB

President Dr William M Howard, 389 Linwood Ave, Buffalo 9  
 Secretary-Treasurer Dr Sheldon B Freeman, 196 Linwood Ave, Buffalo 9  
 Time Second Thursday of each month from October to May

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President Each member, in alphabetical order  
 Secretary Dr Douglas Chamberlain, Providence Bldg, Chattanooga, Tenn  
 Place Mountain City Club Time Second Thursday of each month from  
 September to May

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 Place Continental Hotel, 505 N Michigan Ave Time Third Monday of each  
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 Secretary Dr A A Levin, 441 Vine St, Cincinnati  
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